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October 15-16, 2018 | Tokyo, Japan

DAY 1

Keynote Forum

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John Ebnezar, Biomed Res 2018, Volume 29 | DOI: 10.4066/biomedicalresearch-C5-012

CONVENTIONAL VS. WHOLISTIC THERAPY, WHICH IS THE BETTER OPTION IN THE MANAGEMENT OF KNEE OSTEOARTHRITIS ASSOCIATED WITH OBESITY?

John Ebnezar
Parimala Health Care Services, India

Biography

John Ebnezar is an internationally renowned orthopedic surgeon, passionate about creating, conceptualizing, implementing preventive new orthopedic health awareness modules with an aim to propagate low cost orthopedic health care. He is specialized in trauma, spine, geriatric orthopedics and sports medicine. He holds Guinness World Records both for academics (2010) and social service (2015), only orthopedic surgeon in the world to do so. He is a PhD in yoga, involved in six original-yoga researches, won Best Research Award from SVyasa Yoga University (2012) for his work on knee arthritis and role of yoga in fracture healing (2010). He has pioneered a new treatment method, wholistic orthopedics, by blending modern orthopedics with Indian Yoga, which is simple, cheap, effective alternative for patients for whom knee replacement is not an option and for patients with modern life style orthopedic problems and has redefined the way orthopedic ailments are treated across the globe. He has authored more than 200 books in Orthopedics, a World Record, and has more than 60 scientific publications which has been cited more than 150 times.

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Note:

Osteoarthritis knee is the most common joint disorder affecting nearly 10% of the world population. There are several non-modifiable and modifiable risk factors for OA Knees with obesity being the greatest modifiable risk factor. How excess weight influences OA is not clear. Obesity has both a mechanical and inflammatory component in the development and worsening of knee arthritis. Traditionally osteoarthritis knees have been treated with non-pharmacological, pharmacological and surgical methods. When OA Knee is associated with obesity where the situation is far more complex, these treatment methods are not effective. There is a need for paradigm shift from conventional to comprehensive treatment. A patient with OA and obesity knees suffers and not in isolation and the traditional treatment methods alone may not be enough. Yoga with its multidimensional approach of body, mind and soul implications could be an answer. Extensive research on the role of yoga as an add on in the treatment of OA knees associated with obesity has shown excellent to good results. My research studies were picked up by American Association of Orthopedic Surgeons (AAOS) in formulating the 2013 Non-Arthroplasty treatment guidelines for OA Knees. A broad-based treatment called wholistic treatment keeping yoga as the central option in the treatment of OA Knees and Obesity seems to be the best option.

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Orlando Leite de Carvalho

The Santa Marcelina Hospital, Brazil

Biography

Orlando Leite de Carvalho has completed his Medical College from Amazon Federal Medical College, and he was specialist in Endocrinology from Gama Filho University. He is the Director of Santa Marcelina Hospital, Porto Velho. He is the Coordinator of The State Service of Endocrinology, Diabetic Foot Service Coordinator, Professor of Medical School São Lucas, Porto Velho, Rondônia , Amazon, Brazil.

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DIABETES MELLITUS AND LEPROSY: NEW EDUCATION PROTOCOL IN FOOT AT RISK AT THE SANTA MARCELINA HOSPITAL, AMAZON, BRAZIL

Objective: To apply an intensive and multidisciplinary education protocol to decrease, improve, delay or cancel the beginning of neuropathy and the manifestation of lesions in diabetic patients.

Methodology: This is a cross-sectional descriptive study carried out at the Diabetes Mellitus Outpatient Clinic and ward of Santa Marcelina Hospital in Porto Velho. This research was based on cases of patients with Diabetes and Diabetics with Leprosy. The criteria used to include the patients were: being treated with insulin therapy, not to be amputated, being on high medication of the leprosy now of the evaluation and to present nutritional risk classification by the screening. The population was divided into two groups of fifteen patients: eight diabetic patients, four male and four females. Seven diabetics associated with leprosy were free males and three females.

Results & Discussion: Group A, called the intensive care group, began diabetes education work with medical, nutritional and rehabilitation guidelines by a multidisciplinary team. Group B, called conventional care, received the same guidelines in outpatient care and the monitoring followed the quarterly protocol. Both groups were evaluated and reassessed for a period of 180 days in the outpatient clinic. Group A consisted of eight (100%) patients, four (50%) diabetics and four (50%) diabetics and leprosy patients.

Conclusion: This research highlights, once again, the importance of integration among the specialties. Therefore, experimental models of multidisciplinary clinic outpatient of clinics should be encouraged in clinical practice to promote a more comprehensive care on different functional aspects. Intensive education in diabetes showed an improvement in the sensitivity, healing and nutritional status of the patients, leading to an improvement in quality of life and disability, reducing or delaying the inception of neurological complications. The intensive form of the protocol demonstrated a 100% improvement in patients in group A.

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Uraiwan Intamaso
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Biography

Uraiwan Intamaso have completed her PhD from Montana State University, USA. Currently, she is an Associate Professor in Microbiology, Division of Medical Technology, Faculty of Allied Health Sciences, Burapha University, Thailand. Her scientific fields mainly focus in Molecular Virology and now research interests expand to an innovative approach in viral detection and vaccines. She was invited as a keynote speaker on the topic advance and innovations to detect enteric viruses in seafood and a speaker on the topic the emergence of uncommon genotypes of rotaviruses in Thailand at the 7th International Conference on Agriculture, Chemical, Biological and Environmental Sciences on 22-24 May 2017 at Kuala Lumpur, Malaysia. She enjoys solving scientific problems and shares research knowledge with other scientists.

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CONSTRUCTION AND CHARACTERIZATION OF YEAST DISPLAY OF VIRAL CAPSID PROTEIN: A PRELIMINARY IMPLICATION FOR PRODUCTION OF ORAL VACCINE AGAINST NERVOUS NECROSIS VIRUS

Nervous necrosis virus (NNV) causes viral nervous necrosis that often reaches higher than 99% mortality rate in hatchery-reared larvae and juveniles. There are still no effective vaccines currently available for NNV. Yeast surface display of capsid proteins of red-grouper-nervous- necrosis virus (RG-NNV) was constructed aimed at developing an oral vaccine in fish. RG-NNV infection in fingerlings or juveniles that showed clinical signs of abnormal swimming patterns was proved by RT-PCR and DNA sequencing. The 2,100 bp of DNA fragment containing RNA2 capsid protein of RG-NNV fused to AGα1 of S *cerevisiae* in linearized pPIC9K vector was electroporated into P *pastoris* GS115. Yeast auxotroph isolates were preliminary selected by histidine-producing ability and geneticin resistance. The recombinant yeasts were cultured in buffered minimal glycerol-complex medium (BMGY) and induced with 0.5% methanol in buffered minimal methanol complex medium (BMMY). Only 50% of the expression of the fusion proteins was detected by Western blot. Immunofluorescence labeling confirmed the correct localization and the predicted tertiary structure proposed the exposed conformation of the fusion protein on the cell wall. Optimization of protein expression is required for fully surface protein expression before the evaluation of the possible use of the capsid protein displayed yeast as an oral vaccine against RG-NNV infection.

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Patricia Avila Fabrini
Santhè Clinic, Brazil

Biography

Patricia Avila Fabrini has an in fusional center in Belo Horizonte, Minas Gerais, Brazil. She has her expertise in immunobiological drugs and in her center of treatment, she also has a vaccination center for the safety use of these drugs that acts in the immune systems of patients.

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VACCINATION IN PATIENTS IN USE OF IMMUNOBIOLOGICAL DRUGS FOR IMMUNE MEDIATED DISORDERS

Immune mediated inflammatory disease (IMID) is a concept used to describe a group of conditions that share common inflammatory pathways. Encompassing disorders as ankylosing spondylitis, multiple sclerosis, psoriasis, arthritis psoriatic, rheumatoid arthritis, hidradenitis suppurativa and inflammatory bowel diseases, the immune dysregulation may afflict any organ system and result in significant morbidity, reduced quality of life (QoL) and premature death. Although the aetiology of these conditions is unknown, advances in molecular research have revealed that an imbalance in inflammatory cytokines is central to their pathogenesis. The most convincing evidence linking the pathophysiology and treatment of autoimmune diseases has been demonstrated with the tumour necrosis factor α (TNFα) inhibitors. The therapeutic aims for the drugs used for the treatment IMIDs are: to gain rapid control of inflammation, prevent tissue damage, improve QoL and, if possible, achieve long term disease remission. This drug is named immunobiological drugs. Their use is related to immunosuppression, and the patient who will be submitted to this kind of treatment needs to be vaccinated. However, severe complications have followed vaccination with live, attenuated virus vaccines and live bacterial vaccines among immunocompromised patients. In general, these patients should not receive live vaccines. The aim of the present study is to standardize conduct of vaccination in patients using immunobiological drugs.

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PRE-CLINICAL & CLINICAL DEVELOPMENT OF BIOSIMILAR INSULINS/INSULIN ANALOGUES: THE CLINICAL IMPLICATIONS OF CRITERIA FOR SIMILARITY

Agam Shah
Wockhardt Ltd, India

Biography

Agam Shah has rich professional experience of nearly 15 years in clinical development, medical affairs and academics. He has been an avid Clinical Research Physician with numerous scientific publication and presentations to his name. He has comprehensive experience of clinical development of biosimilars, complex generics and vaccine products.

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Introduction: Akin to generic product development through pharmaceutical equivalence followed by bioequivalence compared to reference medicinal product to ascertain similar safety and efficacy, biosimilar insulin/analogue product (BIP) development includes physio-chemical-biological characterization followed by human PK-PD study and safety-efficacy-immunogenicity study compared to reference insulin product (RIP) to ascertain the same. Although, development of multiple biosimilar insulin products has been undertaken throughout the world, clarity about the clinical implications of the results of these studies is not much discussed.

Objective: To assess the clinical implications of pre-clinical and clinical studies undertaken on BIP to establish its similarity to their RIP in terms of their results.

Methods: Results of studies conducted by Wockhardt Ltd. for development of their BIP of insulin glargine as per in comparison to RIP were evaluated to assess their criteria for similarity in the context of clinical implications.

Results: Results of the *in vitro* receptor binding assays, *in vitro* receptor auto-phosphorylation, *in vitro* metabolic assays and *in vivo* PD studies indicate that BIP is comparable to the RIP in the potential for glucose lowering effects. Whereas, results of the *in vitro* mutagenicity assays, sub-chronic toxicity study indicate that BIP is comparable to the RIP in potential for toxicities, pharmacokinetics and immunogenicity. Results of human PK-PD studies conducted in healthy volunteer and type 1 diabetics under euglycemic clamp settings proved that BIP is bioequivalent to the RIP in glucose lowering effect and insulin glargine exposure. Whereas, results of comparative safety-efficacy-immunogenicity studies in type 1 and type 2 diabetics confirmed that BIP is non-inferior to RIP in glycaemic control as well as comparable to it in hypoglycaemic events, other adverse events and immunogenicity.

Conclusion: Pre-clinical and clinical development data on BIP offers comprehensive information of clinical PK-PD, safety, efficacy and immunogenicity in comparison to RIP to understand clinical implications of BIP's use in practice.

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Sarah Ferber, Biomed Res 2018, Volume 29 | DOI: 10.4066/biomedicalresearch-C5-012

Sarah Ferber
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Biography

Sarah Ferber is graduated at the Technion under the supervision of Prof. Hershko and Prof. Ciechanover on revealing the Biology of the ubiquitin system for protein degradation (Nobel Prize in 2004). She completed her post-Doctoral studies at Harvard Medical School on the regulation of insulin secretion and moved to Diabetes Cell Therapy in UTSW-Dallas TX. She established her own research lab at Sheba Medical ctr. Israel and was the first to demonstrate liver to pancreas trans differentiation *in vivo* and in human tissues *in vitro* for generating an autologous insulin producing tissue. She has since published in leading journals, and her papers were cited >2700 times. She has been serving as an editorial board member of reputed journals and on the Israeli and the European boards of Gene and Cell Therapy Societies. She serves as Orgenesis' CSO and founder and is the inventor of >10 patents on adult cells reprogramming.

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AUTOLOGOUS CELL REPLACEMENT THERAPY FOR DIABETIC PATIENTS BY LIVER TRANSDIFFERENTIATION

Trans differentiation is the direct reprogramming of adult cells into alternate cell types with different function. Liver to pancreas transdifferentiation (TD) induced by ectopic expression of pancreatic transcription factors (pTFs) was first described by our group both *in vivo* and in human liver cells *in vitro*. The keynote lecture will disclose our understanding of the mechanism of liver to pancreas TD and will describe this approach's industrial implementation as an autologous cell replacement therapy for diabetic patients. Our data suggest that TD occurs in predisposed liver cells that display specific characteristics. Moreover, TD-propensity can be extended to most of the cells by epigenetic manipulations, hence, increasing the trans differentiation efficiency. Using primary cultures of liver derived from >20 human donors we have identified a sub-population of human liver cells that are persistently predisposed to undergo TD (5-15% of the cells). Upon ectopic pTFs expression, 70% of the predisposed liver cells produced and secreted the processed hormone in a glucose-regulated manner. Epigenetic analyses suggested that pancreatic genes' chromatin is more transcrpition-permissive in TD-predisposed than in recalcitrant liver cells. TD-predisposed liver cells display a reduced level of DNA methylation which further decreases upon the induction of reprogramming. Using epigenetic modifiers, we could convert TD-resistant liver cells into TD-permissive cells. Moreover, *in vitro* culturing of the AIP cells in a 3D organoid manner, and their exposure to a suitable and relevant niche, increased the transdifferentiated liver cells maturation insulin production. In summary, pancreatic TD is restricted to a specific cell population within the adult liver tissue, which harbors obligatory signaling patterns and specifically permissive epigenome. The extension of TD-propensity to most of the cells in culture/tissue, is expected to dramatically increase this process efficiency bringing it closer to its therapeutic implementation, as an autologous cell replacement therapy for diabetic patients.

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Biography

Saida Marzanova has completed her PhD at the age of 25 years from Moscow State Academy of Veterinary Medicine and Biotechnology-MVA K. I. Skryabin, Russia. She is the Associate Professor of Moscow State Academy of Veterinary Medicine and Biotechnology-MVA K. I. Skryabin, Russia. She has over 50 publications that have been cited over 25 times, and her publication H-index is 3 and has been serving as an editorial board member of reputed Journal "Veterinary Medicine".

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THE PRESENT AND FUTURE OF VACCINEAL PREVENTION OF ANIMAL BRUCELLOSIS

The effectiveness of corrective measures for brucellosis is largely determined by the quality of epidemiological surveillance and the effectiveness of vaccine prevention. Used live vaccines do not fully protect against infection, at the same time they pose a potential risk of Brucella infection in animals with low immune resistance and post-vaccination complications and pose a danger to livestock breeders and the population consuming untreated products from vaccinated animals. Inactivated vaccines did not find practical application due to insufficient efficacy and high reactogenicity. Considering that vaccination is the basis for the prevention of Brucella infection, we conducted studies on the selection of strains, developed and experimentally tested a split conjugated biosafe vaccine based on immunogenically active subcellular and soluble peptides of three Brucella strains: *B.melitensis* and two strains of *Brucella bovis* biotype. To stimulate specific immunity, Brucella antigens were conjugated to an immunoprotector. The immunoprotector was obtained from a culture of B lymphocytes sensitized with Brucella antigens. Activity control was assessed by immunostimulating of the mechanisms of cellular and humoral immunity and immunogenic activity of the vaccine in guinea pigs. The immunogenic activity of the declared vaccine was studied on guinea pigs weighing 300-400 g, which were subcutaneously injected into the groin area with test specimens of vaccines at a dose of 0.5 cm^3. After four weeks vaccinated guinea pigs were infected with a virulent culture of B. bovis 10 in an infectious dose (ID). At the same time, non-vaccinated (control) guinea pigs were infected. 30 days after infection, guinea pigs were killed and bacteriological seeding of lymph nodes and organs on Brucella agar and Brucella broth was performed. Seeding was sterile in 100% of vaccinated guinea pigs. In seeding from control unvaccinated guinea pigs in 100% of cases, a culture of Brucella of the infecting strain was isolated. As, a result, immunization of the split-conjugated brucellosis vaccine activates the cellular and humoral immune response, enhancing the induction of specific antibodies. Advantages of a split-conjugated vaccine: biosafety, protection of immunized animals from infection with brucella during experimental infection, reliably exceeds the specific efficiency of live anti-brucella vaccines from strains B. abortus 19 and B. melitensis Rev-1.

Note: