

WAYNE STATE UNIVERSITY

EUGENE APPLEBAUM
COLLEGE OF PHARMACY
AND HEALTH SCIENCES

9th Annual Research Forum

2012





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Agenda:

8:00 AM – 9:00 AM	Poster Setup
9:00 AM – 11:00 AM	Student Poster Judging
11:00 AM	Welcome: Lloyd Y. Young, Pharm. D., Dean
11:05 AM	Introduction to Speaker: Deepak K. Bhalla, Ph. D Associate Dean for Research
11:15 AM - 12:00 PM	Key Note Speaker: Anthony Atala, M.D. “Regenerative Medicine: Current Concepts and Changing Trends”
12:00 PM	Faculty Research Recognition and Student/Postdoc Poster Awards: Dean Lloyd Y. Young
12:30 PM	Lunch
12:30 PM – 3:00 PM	Poster Display and Presentation

Key Note Speaker: Anthony Atala, M.D.



Anthony Atala, M.D., is the Director of the Wake Forest Institute for Regenerative Medicine, and the W.H. Boyce Professor and Chair of the Department of Urology at Wake Forest University. He is a practicing surgeon and a researcher whose work focuses on growing new human cells, tissues and organs.

Dr. Atala is a recipient of many prestigious awards, including the US Congress funded Christopher Columbus Foundation Award, bestowed on a living American working on a discovery that will significantly affect society, the World Technology Award in Health and Medicine, presented to individuals achieving significant, lasting progress, the Samuel D. Gross Prize, awarded every 5 years to a national leading surgical researcher by the Philadelphia Academy of Surgery, the Barringer Medal from the American Association of Genitourinary Surgeons, and the Gold Cystoscope award from the American Urological Association for advances in the field. His other honors include election in 2011 to the Institute of Medicine of the National Academy of Sciences and recognition by

Scientific American as a Medical Treatments Leader of the Year for his contributions to the fields of cell, tissue and organ regeneration. In 2007 Dr. Atala's work was listed as Time Magazine's top 10 medical breakthroughs of the year, and as Discover Magazine's Number 1 Top Science Story of the Year in the field of medicine. A Time Magazine poll ranked Dr. Atala as the 56th most influential person of the year in 2007. In 2009 he was featured in U.S. News & World Report as one of 14 Pioneers of Medical Progress in the 21st Century, and his work in 2010 was listed by Smithsonian Magazine as one of 40 things to know about the next 40 years. His work was listed in the Huffington post as one of 18 great ideas of 2011, and in Time Magazine as one of the top 5 medical breakthroughs of the year.

Dr. Atala has led or served several national professional and government committees, including the National Institutes of Health working group on Cells and Developmental Biology, the National Institutes of Health Bioengineering Consortium, and the National Cancer Institute's Advisory Board. He heads a team of approximately 300 physicians and researchers. Ten applications of technologies developed in Dr. Atala's laboratory have been used clinically. He is the editor of twelve books and has published more than 300 journal articles. He has applied for or received over 200 national and international patents.

Dr. Atala serves in various capacities on the Editorial Boards of many journals. He is the Editor-in-Chief of three prestigious journals and Associate Editor of four other journals. He also serves as the Executive Board Member, Section Editor or Member of the Editorial Board on more than a dozen journals in the areas of Tissue Engineering, Regenerative Medicine and Urology.

Research Forum



Abstracts

Abstract No. 1 (Student_Graduate)

Title

The Design and Implementation of a Multidisciplinary, Student-Run, Free Diabetes Education Wellness Clinic

Affiliations

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University and Diabetes Education Wellness Clinic

Authors

Kristin Perry, Sarah Mahoney, Margi Shah, Kathryn Hurren Pharm.D.

Abstract

Introduction and Purpose. Diabetes is an epidemic that relies on patients' knowledge and ability to perform several daily self-management activities. To fulfill this unmet need for underserved patients in our community, a multidisciplinary, student-run, free Diabetes Education Wellness Clinic (DWC) was created by students and faculty from pharmacy, physical therapy, occupational therapy, and social work disciplines in January 2011. The mission of DWC is twofold: to provide high-quality diabetes education to empower and improve the health of underserved patients with or at high-risk for type 2 diabetes and to provide students with an opportunity to practice patient care and develop communication, empathy and teamwork skills.

Patients. The DWC was formed in partnership with S.A.Y. Detroit Family Health Clinic in Highland Park, Michigan. Patients are referred by their primary care physician (PCP) or are identified by chart review and contacted by phone. Patients participating in this clinic are underserved women with prediabetes or type 2

diabetes.

Design. The clinic is organized into themed tables through which patients rotate in order to provide patients with one-on-one care. Basic patient information is collected from the medical record. At the general diabetes education table, students from any discipline provide counseling about the pathophysiology of diabetes, complications, goals, and glucometer use and monitor blood pressure. Occupational therapy students monitor vision acuity and sensory perception and provide education regarding vision and sensation deficit management and coping with diabetes. Physical Therapy students demonstrate exercises, recommend home exercise programs and teach about daily foot care. Pharmacy students provide medication counseling, identifies drug related problems, assesses drug adherence, and review glucose logbooks. Students with a dietetic education background offer meal plan assistance. Recommendations regarding lab work, medications or referrals are provided to the patient's PCP.

Implementation. The DWC is held on the first and third Monday of every month from 5 pm to approximately 8 pm. On average 4 to 6 patients per date attend and our patient base is expanding with more active recruitment. In order to offer comprehensive counseling, each patient spends approximately ninety minutes at the clinic. Each clinic is run by student volunteers with approximately 2-4 students at each table and faculty preceptors and/or community clinician preceptors from each discipline are present. Additional descriptive data including mean patient satisfaction scores, enrollment in patient assistance programs, patient time spent at each table, and physician recommendations and acceptance will be reported.

Abstract No. 2 (Student_Graduate)

Title

Dendritic Polycationic Prodrugs as Gene Delivery Vectors

Affiliations

1 Department of Pharmaceutical Sciences,
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Wayne State University School of Medicine
3 Karmanos Cancer Institute, Detroit, MI 48202

Authors

Yu Zhu¹, Stuart Hazeldine¹, Jing Li¹, Jing Li^{2,3}, David Oupický^{1,3}

Abstract

Clinical application of non-viral gene delivery vectors continues to be hindered by low transfection activity and high toxicity. Here, we propose to overcome the problems by designing biodegradable polymeric prodrugs that can function dually as gene delivery vectors and, after intracellular degradation, as active anticancer agents targeting dysregulated polyamine metabolism. We synthesized dendritic polycations with core-shell structure using polyglycerol (PG) core and amine shell of a polyamine analog drug N1,N11-bisethyl norspermine (BEN). The synthesized PG-BEN is expected to function dually as a gene delivery vector and a prodrug, which can release the active pharmacologic agent BEN known to synergistically augment the activity of TNF-related apoptosis-inducing ligand (TRAIL) in human breast cancer.

Abstract No. 3 (Student_Graduate)

Title

ESTIMATING ELECTROMYOGRAPHIC AND HEART RATE FATIGUE THRESHOLDS FROM A SINGLE TREADMILL TEST

Affiliations

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Authors

Darren R. Guffey, SPT, Bruno J. Gervasi, SPT, Alex A. Maes, SPT, and Moh H. Malek, Ph.D.

Abstract

Introduction: The purposes of this study were to: 1) develop a fatigue threshold (FT) based on electromyography (EMG) and heart rate (HR) responses for treadmill running from a single incremental test ... and 2) propose a new fatigue threshold called the RVEMGFT and RVHRFT.

Methods: Eleven men performed incremental treadmill exercise to exhaustion on a single occasion. The RVEMGFT and RVHRFT were defined as the average of the highest velocity that resulted in a non-significant slope coefficient for the EMG amplitude versus time relationship and the lowest velocity that resulted in a significant positive slope coefficient.

Results: There was a significant ($p < 0.05$) difference between the two thresholds [RVEMGFT = 11.7 ± 0.6 km/h and RVHRFT = 8.3 ± 0.8 km/h].

Discussion: The fatigue threshold for EMG amplitude and heart rate can be determined from a single incremental treadmill test, but differences between cardiac and neuromuscular factors of fatigue.

Abstract No. 4 (Student_Graduate)

Title

Impact of Doctor of Pharmacy Student Interventions on a General Pediatric Service

Affiliations

Pharmacy Practice Eugene Applebaum College of Pharmacy and Health Sciences and Department of Pharmacy, Children's Hospital of Michigan.

Authors

Katia Saleh PharmD Candidate, Dennis Gates, MS, Victoria Tutag Lehr BS Pharm, PharmD

Abstract

Introduction: Doctor of Pharmacy students as part of General Pediatrics rotation at Children's Hospital of Michigan provides medication therapy management on 30 bed general pediatric units. Infants, children and adolescents are at higher risk for drug related morbidity and mortality due to rapidly developing organ systems, unique dosing requirements, and high use of off label medications. The value of pharmacy students' interventions have been shown for adult populations yet no reports of the impact of pharmacy student interventions on a pediatric service. Hypothesis: Student pharmacist's interventions impact morbidity, safety and result in cost avoidance and result in other benefits such as education of the interdisciplinary team. Objectives: 1. To describe the number and types of interventions made by pharmacy students. 2. To evaluate impact of interventions made by pharmacy students measured by improvement in clinical outcomes. Primary Outcome: Therapeutic medication class with the highest number of interventions. Secondary outcomes ... significance of interventions ... type of intervention ... applications to practice Study Design: Pilot prospective descriptive study at Children's Hospital of Michigan. Methods: Interventions collected by 4th year students

(July to September 2012) using standardized forms on daily rounds Monday-Friday during the day shift. Preceptor reviewed interventions and classification as minor, moderate, major significance. Inclusion: Interventions e.g. dosage changes, medication DC or addition, TDM, etc made by student and accepted by the resident. Exclusion: Interventions not accepted by team. Results: Overall n=45 interventions representing 11 therapeutic classes were made on 299 patients. (These were 20% major, 56% moderate and 24% minor significance). Antimicrobials (ceftriaxone 16%), analgesics/opioids (morphine 13%), and antiepileptics (phenobarbital 7%) required the most interventions. Conclusion: Pharmacy students made interventions on 15% of patients admitted to a general pediatric unit. Student interventions have clinical value. Most agents (morphine, ceftriaxone, phenobarbital) involved in an intervention have been associated with ADRs in children according to national reports. In addition, mesalamine was being administered with gastric acid modifiers (PPIs, H2 blockers) which may decrease its efficacy. Student intervention has resulted in a new computer system alert for this drug interaction. Analyses will assess cost savings associated with student interventions, using an interventions log created for this study in the next phase. Data collection is ongoing. Results will be used to focus physician education and research.

Abstract No. 5 (Faculty)

Title

Building a community of leaders - the impact of student organizations on leadership development

Affiliations

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2. Department of Pharmacy Services, Oakwood Hospital and Medical Center, Dearborn MI

Authors

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Abstract

Objective: To assess the impact of involvement in Wayne State University's American Pharmacists Association – Academy of Student Pharmacists (WSU APhA-ASP) Chapter on leadership engagement in other student run organizations and to determine how organizational involvement influenced continued professional leadership development.

Design: WSU's APhA-ASP Chapter created a student-driven organizational community to empower students to utilize leadership skills such as networking, program development, project management, training, marketing, communication, collaboration, and problem-solving to implement patient care projects, membership development, fundraising initiatives, and professionalism programming. Additionally, organization-run activities have provided opportunities for students to fulfill curricular requirements, as well as to network and interact with other students, faculty, and staff at WSU and within the community. Pharmacy practice faculty, pharmaceutical sciences faculty, and volunteer faculty, preceptors, and residents are actively involved in program implementation and supervision in each of the key areas of the organization.

Evaluation: To assess the overall impact of this community on the development of leaders, a survey will be used to establish: 1) the level of student involvement and responsibilities within ASP, 2) how their participation as an ASP member impacted their involvement in other student run organizations and what leadership positions they held within those organizations, 3) explore members' perceptions on leadership skills gained, self-recognition of their contributions and value to the mission of the organization, and 4) the perceptions of new

practitioners regarding the influence of organizational involvement on leadership development.

Assessment: Four hundred ASP student members that were active anytime between September 2009 and July 2012 will be surveyed. Descriptive statistics will be used to assess active and past members' perceptions.

Summary: This program provides students the opportunity to create a culture of leadership that extends beyond the boundaries of an organization. Survey results will offer insight into perceived leadership skills developed through participation in the program.

Abstract No. 6 (Faculty)

Title

Determining Minimal Detectable Change in Two Balance Outcome Measures for Patients with Stroke

Affiliations

Wayne State University

Authors

Vicky Pardo, PT, MHS, DHS ... Allon Goldberg, PT, PhD ... Erin Boguslawski, SPT ... David Genoff, SPT ... Alissa Humes, SPT

Abstract

Purpose/Hypothesis: The Berg Balance Scale (BBS) is a 14-item objective assessment of balance during functional activities. The Activities-specific Balance Confidence Scale (ABC) is a subjective measure of self-confidence in maintaining balance during 16 functional activities. Minimal detectable change (MDC) represents a value for real change that exceeds the chance of variation in measurement. MDC can be used to interpret whether changes in these measures over time represent real change or are within the boundaries of

measurement error. The purpose of this study was to quantify measurement error and MDC in the BBS and the ABC in people who have had a stroke.

Number of Subjects: Ten community-dwelling participants with a history of stroke affecting one side of the body were recruited from the Metro Detroit area.

Materials/Methods: Participants were assessed using the BBS and the ABC on two separate occasions with 2 to 7 days between tests. The intraclass coefficient (ICC 2.1) was computed to assess test-retest reliability of each test. Standard error of measurement (SEM), which quantifies measurement error in absolute values, was calculated as the standard deviation $\times \sqrt{1 - \text{ICC}}$. MDC at a 95% confidence level (MDC95) was calculated as $z \times \text{SEM} \times \sqrt{2}$ where $z=1.96$.

Results: Mean BBS was 41.7, with an ICC of 0.99 (SEM was 1.15, MDC95 was 3.19). Measurement error and MDC 95 expressed as a percentage of mean BBS were 2.76% and 7.65% respectively. Mean ABC was 77.17%, with an ICC of 0.93 (SEM was 5.30, MDC95 was 14.69). Measurement error and MDC95 expressed as a percentage of mean ABC were 6.87% and 19.04% respectively.

Conclusions: The high ICC for the BBS and the ABC suggest high test-retest reliability. The low MDC% for the BBS suggests a high sensitivity to detect real change in performance. The MDC% for the ABC is somewhat higher, but still reflects high sensitivity. The low SEM% for the BBS and the ABC is suggestive of low measurement error and good absolute reliability.

Clinical Relevance: In patients with stroke, real change was computed to be >3.19 points on the BBS and >14.69 on the ABC. These results will assist clinicians and researchers in interpreting whether real change has occurred when comparing repeated measures of BBS and ABC.

Abstract No. 7 (Student_Graduate)

Title

UNDERSTANDING EDUCATION ACCESS AND REFERRAL NEEDS OF PERSONS WITH DEMENTIA AND THEIR CAREGIVERS LIVING IN THE METROPOLITAN DETROIT AREA

Affiliations

Department of Healthcare Sciences, Programs in Occupational Therapy and Physical Therapy, Instructional Technology Research Laboratory, Wayne State University, Detroit, Michigan, 48201

Authors

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Ambily Thomas, SPT,
Rosanne DiZazzo-Miller, DrOT, OTRL
Fredrick D. Pociask, PhD, PT

Abstract

Currently, it is estimated that over 15 million Americans provided 17.4 billion hours of unpaid care for individuals with dementia in 2011. Despite the growing number of informal caregivers, there is a gap in the literature addressing how caregivers of persons with dementia locate and utilize resources to assist with caring for an individual with dementia. Use of a needs assessment in the development or execution of any caregiver training programs has not been found. The purpose of this research study is to understand caregivers' experiences in accessing resources throughout various stages of dementia. Twenty three participants were recruited on a voluntary basis in cooperation with the Alzheimer's Association Greater Michigan Chapter. Each participant completed a single three hour focus group based on diagnosis or role: 1) caregivers for, and persons with early stage dementia, 2) caregivers for persons with middle stage dementia, 3) caregivers for persons with late stage dementia, 4) or subject matter experts. Questions for subject matter experts

included information they thought was absolutely critical for clients with dementia or caregivers to receive, the most sought after information by caregivers, what is most frightening to persons with dementia and caregivers at different stages, and what suggestions they have in making resources more accessible to both caregivers and care recipients. Caregivers for persons in early, middle and late stage dementia were asked questions regarding the educational and training resources used in the past and how they found them, what they considered most and least valuable educationally, as well as other available resources used. Guiding questions were developed by experienced service professionals and used to guide the research. This preliminary data provides us with rich insights needed to develop meaningful survey instruments, to better understand access and resource needs and to support future inquiry that is necessary to understand the lived experiences of care recipients and family caregivers for persons with dementia.

Key words: caregiver, dementia, Alzheimer's, needs assessment, resources, focus group

Abstract No. 8 (Faculty)

Title

Tobacco smoke modulates ozone induced toxicity in the lungs and central nervous system

Affiliations

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Authors

¹Vanitha Bhoopalan, ²Sung Gu Han, ¹Mrudang Shah, ³David Thomas and ¹Deepak Bhalla

Abstract

This study was performed to determine if sequential exposures of rats to ozone (O₃) and tobacco smoke (TS) would produce lung and central nervous system (CNS) injury greater or lesser than that produced by O₃ alone. These studies extend the known effects of O₃ exposures in the lung and brain. Adult (SD) male rats were exposed for a single 3 hr period to: 1) Air (control), 2) O₃ and 3) O₃ followed by TS (O₃/TS). For pulmonary effects, bronchoalveolar lavage (BAL) was performed, and BAL cells and fluid were analyzed. Data revealed a significant increase in polymorphonuclear leukocytes (PMN), and total BAL protein in the O₃ group compared to controls, reflecting inflammatory and toxic effects of O₃. However, a subsequent exposure to TS attenuated PMN infiltration into the airspaces and subsequent recovery in the BAL. A similar reduction was also observed for BAL protein and albumin in the O₃/TS group, but it was not statistically significant. We also observed a significant increase in BAL total antioxidant capacity in the O₃ group compared to that in the controls, suggesting development of protective mechanisms for oxidative stress damage from O₃. Exposure to TS attenuated the levels of total antioxidant capacity, but the reduction was not statistically significant. Lung tissue protein analysis further showed a significant reduction of extracellular superoxide dismutase (EC-SOD) in O₃ and O₃/TS groups and catalase in O₃/TS group, compared to the control. However, TS did not further alter O₃-induced protein expression. However, TS did not further alter O₃- induced protein expression. For effects in the CNS, we measured striatal dopamine levels in the O₃ and O₃/TS groups by HPLC with electrochemical detection. O₃ reduced striatal dopamine content, while the subsequent TS exposure afforded a non-significant protection. Overall, the results show that the toxicity of O₃ in the lung and brain are modulated by exposure to TS, and the attenuation is contrary to the synergistic toxicity predicted for TS and O₃. The results are comparable to the attenuated responses following sequential exposures to carbon nanotubes and O₃ reported in our previous

studies, suggesting limited cross-tolerance following such exposures.

Abstract No. 9 (Faculty)

Title

Assessing the Impact of a Heparin Induced Thrombocytopenia Recognition and Management Protocol

Affiliations

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Authors

John M Koerber, Pharm.D.1*, Trupti P Mehta, Pharm.D.1*, Lisa L Forsyth, Pharm.D.1*, Lindsey Corbets, Pharm.D.1*, Elizabeth Conger1*, Joan C. Mattson, MD2, Rajul Parikh, MD3*, Elizabeth Sykes, MD2* and Maureen A Smythe, Pharm.D.1,4*

Abstract

Heparin-induced thrombocytopenia (HIT) is an immune mediated adverse reaction to heparin which results in significant patient morbidity. A comprehensive HIT Recognition and Management Protocol was developed. The overall goal of this project was to assess the impact of protocol implementation on HIT management.

A retrospective observational cohort study using a pre – post design was used. Patients started on direct thrombin inhibitor therapy (DTI) from September 1st 2009- February 28th 2010 for suspected/confirmed HIT composed the pre implementation group while those started on DTI therapy from November 1st 2010 – April 30th 2011 composed the post implementation group. Data extraction involved demographic,

clinical, laboratory and pharmacy data. DTI initiation within 12 hours of HIT laboratory testing in patients with an intermediate to high 4Ts score was assessed. Additional endpoints included appropriate discontinuation of DTI therapy defined as discontinuation within 12 hours of a negative PF4/heparin ELISA or within 12 hours of a negative SRA in patients with a positive PF4/heparin ELISA with an optical density below 2. Hours of inappropriate continuation of DTI therapy and appropriate warfarin transition were also assessed. T- test, Chi square and Mann Whitney U were used to analyze data with a level of significance set at $p < 0.05$.

A total of 61 patients received DTI therapy for suspected/confirmed HIT in the pre period compared to 46 in the post period. DTI initiation within 12 hours of a PF4/heparin ELISA order for those with an intermediate-high 4T score occurred in 8/31 (25.8%) of pre patients and 24/31 (77.4%) of post patients, $p < 0.0001$.

Appropriate discontinuation of DTI therapy after a negative PF4/heparin ELISA occurred in 5/23 (21.7%) of pre patients and 12/26 (46.2%) of post patients, $p = 0.07$. The median number of hours of inappropriate DTI continuation/patient after a negative PF4/heparin ELISA in the pre versus post periods were 99.6 and 25.1 hours respectively, $p = 0.04$. Appropriate discontinuation of DTI therapy after a negative SRA occurred in 2/13 (15.4%) pre and 2/9 (22.2%) post patients, $p = 0.12$.

Seventeen patients in the pre and 10 in the post period were transitioned to warfarin for HIT. Initiation occurred after platelet count recovery to $150 \times 10^9/L$ in 11/17 (64.7%) of pre and 7/10 (70%) of post patients, $p = 0.78$. The initial warfarin dose was $< 5mg$ in 15/17 (88.2%) of pre and 10/10 (100%) of post patients, $p = 0.26$. A minimum 5 day overlap of DTI and warfarin therapy occurred in 11/16 (68.8%) pre and 8/9 (88.9%) of post patients, $p = 0.26$.

Implementation of the HIT protocol improved the timely initiation of DTI therapy in those with an intermediate-high 4Ts score and was successful in promoting appropriate discontinuation of DTI therapy after a negative PF4/heparin ELISA test. Automatic send out SRA testing did not demonstrate a benefit in promoting discontinuation of therapy in those

with a positive PF4/heparin ELISA and a negative SRA.

Abstract No. 10 (Post_Doctoral_Fellow)

Title

Early Experience with Ceftaroline Fosamil Therapy at an Academic Hospital System

Affiliations

Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy and Health Sciences ... Detroit Medical Center ... Wayne State University School of Medicine, Detroit, MI

Authors

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Abstract

Background: The US Food & Drug Administration (FDA) recently approved ceftaroline fosamil (CPT), a cephalosporin, for acute bacterial skin and skin structure infections (ABSSSI) & community-acquired bacterial pneumonia (CABP). CPT is indicated for ABSSSI caused by *S. aureus* (SA) infections including methicillin-susceptible & resistant SA (MSSA & MRSA, respectively). Currently there is limited evidence regarding the use CPT for other infections. The objective of this evaluation is to describe the outcomes of patients (pts) treated with CPT for various infections. **Methods:** A retrospective cohort review of pts who received > 48 hours of CPT at the Detroit Medical Center from January 2011-July 2012. Clinical & microbiological outcomes were analyzed. Clinical cure (CC) defined as infection resolved at the end of CPT therapy & no

additional therapy needed.

Results: 72 pts were treated with CPT for various infections: 47% with bacteremia (including 10 endocarditis, 12 pneumonia, 6 ABSSSI, 2 spinal abscesses, & 3 IV catheter-related infections), & 53% without bacteremia (21 pneumonia & 6 ABSSSI). 35% (25/72) patients were treated within its FDA label. Median APACHE II score was 11 (interquartile range [IQR] 6.25-15). 86% (62/72) pts had positive cultures, 81.9% were SA (49 MRSA & 10 MSSA) infections. There were 33 SA bacteremia (SAB): 5 MSSA, 1 hVISA, & 1 VISA. 29% (18/62) were polymicrobial with Gram-negative bacteria. Median total length of stay was 13.5 days (7.25-24.75) & median duration of CPT therapy was 5.5 days (3-12.75). The median CPT MIC for SA was 0.5 mg/L (0.5-1). The most common CPT dosage was 600mg Q12h, and was adjusted for renal function. The median length of time to clearance of SAB was 3 days (1-5.25) from the start of CPT. 93% (63/68) achieved CC or improvement at the end of CPT therapy. 6 pts expired in the hospital where 1 had organism persistence, 3 had microbiologic cure & the remaining 2 had no follow up cultures. 13 pts were re-admitted within 30 days after discharge, 6 had re-admission for the same infection. **Conclusions:** The majority of pts with SA infections treated with CPT had favorable outcomes. Further research is necessary to clarify its clinical role in these infection types outside its FDA approved label.

Abstract No. 11 (Student_Graduate)

Title

Upregulation of phagocyte-like NADPH oxidase by cytokines in pancreatic β ... -cells: Attenuation of oxidative and nitrosative stress by 2-bromopalmitate

Affiliations

β ... -Cell Biochemistry Laboratory, John D. Dingell VA Medical Center, and Department of

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Authors

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Timothy Hadden (PhD)
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Abstract

Phagocyte-like NADPH oxidase (Nox2) has been shown to play regulatory roles in the metabolic dysfunction of the islet β ... -cell under the duress of glucolipotoxic conditions and exposure to proinflammatory cytokines. However, the precise mechanisms underlying Nox2 activation by these stimuli remain less understood. To this end, we report a time-dependent phosphorylation of p47phox, a cytosolic subunit of Nox2, by cytomix (IL-1 β ... +TNF α ... +IFN γ ...) in insulin-secreting INS-1 832/13 cells. Furthermore, cytomix induced the expression of gp91phox, a membrane component of Nox2. 2-Bromopalmitate (2-BP), a known inhibitor of protein palmitoylation, markedly attenuated cytokine-induced, Nox2-mediated reactive oxygen species (ROS) generation and inducible nitric oxide synthase-mediated nitric oxide (NO) generation. Together, our findings identify palmitoyltransferase as a target for inhibition of cytomix-induced oxidative (ROS generation) and nitrosative (NO generation) stress in the pancreatic β ... -cell.

Abstract No. 12 (Faculty)

Title

Medication use by Patients with Chronic Neck Pain: Risk or Benefit?

Affiliations

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2. University of Michigan, Ann Arbor
3. Department of Physical Therapy, EACPHS, WSU

Authors

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Mary Biglin BS Candidate
Kim Dunleavy PhD Associate Professor1

Abstract

Background: Chronic neck pain (CNP) a common and potentially disabling condition causes individuals to seek relief from analgesics, supplements, and alternative therapies along with physical therapy or exercise. Medications for co-morbidities risk interactions with over-the-counter (OTC) drugs or supplements. There is a paucity of data describing medication utilization, safety and efficacy for CNP. Aims: Observational study of medication utilization by individuals > 50 years with CNP conducted to: 1) describe frequencies of medications and supplements used for CNP and co-morbidities ... 2) identify potential for drug related problems (DRPs) Methods: WSU IRB approved as part of larger investigation of therapeutic exercise for CNP. Participants completed: 1) medication questionnaires 2) pain intensity ratings (NRS) before and after taking analgesics 3) average pain during past week 4) worst pain and 5) Neck Disability Index (NDI). Inappropriate dosing, potential drug interactions and other DRPs identified by review of individual drug regimens. Results: n=43 (age 59 \pm 5.4 ... 50-70 years), (88% female) participants enrolled with mild to moderate neck disability (NDI 12.8 (SD 5.9, range 2-27/50). Major self-reported cervical diagnosis was arthritis (28/42, 66.7%) with (11.9% ... 5/43) reporting cervical stenosis or whiplash history. Participants took 1 to 21 (4.4 \pm 4.2) medications daily (94% for neck pain). Neck pain medications included non-steroidal anti-inflammatory drugs (NSAIDs) (48%),

acetaminophen (24%), aspirin (15%), opioids (14%), skeletal muscle relaxants (9%), supplements (11%) and herbals (4%). Comorbidities for 98% included: arthritis elsewhere (50%), thyroid disease (26%), HTN (22%), gastrointestinal distress (19%), depression (15%), anxiety and insomnia (11% each). Co-morbid medications used by 80% included: NSAIDs (30%) ... antihypertensives (21%) thyroid hormones (16%), sedative hypnotics (11%), benzodiazepines (9%) ... proton-pump inhibitors and H2 blockers (19%). Vitamins (e.g.D MVI,niacin)(49%), elements (calcium, iron, magnesium, zinc) (7%) ... and supplements (probiotics, omega-3) (9%) taken daily. Dose information was appropriate 82% (28/34) Potential drug interactions identified 54% (23/43) included: fall risk (44%) ... gastric toxicity (23%) ... additive sedation (20%), duplicate analgesics (11%) ... decreased hypertensive effect (4%). Twenty eight percent had >1 prescriber and 70% self-medicated. Number of prescribers were associated with greater number daily medications (p=0.01 ... r=0.37) and longer medication use (p=0.03 ... r=0.33). Average pain before analgesic use was 6.5/10 (2-10), with 48% reduction to 3.0 (0-7.5). 22% (9/41) obtained complete relief with medication. Conclusions: Majority of participants used medications for neck pain (94%). NSAIDS the most frequently used analgesic despite limited effectiveness for CNP. These high functioning adults reported comorbidities contributing to large number of daily medications with possible drug interactions in 50% of sample. Self-medication common with drug interaction risk. Not all participants experienced complete relief of pain after medication ... however, 48% decrease exceeds minimum 30% reduction for neuropathic pain meeting an appropriate 50% reduction. Considerations for improving analgesia include adjuncts (gabapentanoids) and optimizing analgesic dosage regimens. Limitations included self-reported medication use and adverse effects without verification of adherence. Results will be used to develop an interdisciplinary assessment for detecting analgesic overuse, drug interactions, adverse effects and increase knowledge of medication use in CNP

population.

Abstract No. 13 (Faculty)

Title

The Influence of Postural Core Activation Training on Gait and Balance in Patients Post-Stroke: A Case Series

Affiliations

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Abstract

Background and Purpose: Traditional post-stroke rehabilitation has mainly focused on restoring independence in gait and extremity function, but the development of greater trunk stability should not be overlooked by therapists. Improving trunk stability post-stroke may lead to an improved ability to coordinate movement sequences of both the trunk and limbs and ultimately improve performance of daily activities. There is no current research that examines the effect of an exercise program that focuses on

improving core stability for populations post-stroke. The purpose of this case series was to examine the effects of a postural core activation program on people with stroke. Case Description: Three individuals (aged 39, 48 and 69) with right hemiparesis due to a chronic stroke participated in this study. Participants attended 12 hour-long training sessions (2x/wk for 6 weeks). Gait parameters (gait symmetry, step length, single leg stance, and gait velocity), the BalanceMaster Limits of Stability (LOS) and weight bearing tests, and the Step Test were assessed twice pre-intervention (3 weeks prior and day 1 of intervention) and once post-intervention. Outcomes: Each participant completed 12 hour-long core activation exercise sessions. All participants demonstrated improvements in movement velocity (LOS) after the intervention. Two of the three participants improved on the Step Test, reaction time (LOS), and maximal excursion (LOS). Outcome measures that did not show improvements were end-point excursion (LOS), percentage weight bearing (BalanceMaster), and most of the gait parameters (single leg stance, gait velocity and step length). Discussion: These findings suggest that 12 sessions of core activation exercises can positively affect movement velocity, reaction time, maximal excursion and performance on the Step Test in people with stroke. It appears that the LOS Test on the BalanceMaster and the Step Test were appropriate outcome measures, whereas the gait parameters on the GaitRite did not capture changes from pre- to post-intervention. Future studies should consider using the LOS and Step Tests in a larger sample of participants with stroke. (320 words)

Abstract No. 14 ()

Title

Development and evaluation of anti-oligomeric and/or anti-fibrillar activity of potential inhibitors of α ... -synuclein aggregation for the treatment of Parkinson's disease.

Affiliations

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Authors

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Aloke Dutta, Ph.D.

Abstract

Around 60,000 people are diagnosed with Parkinson's disease (PD) every year in the United States, with an estimated 7 to 10 million people worldwide suffering from the disease. PD is a progressive neurodegenerative disorder, characterized by a gradual loss of dopaminergic neurons in the substantia nigra region of the midbrain. The major pathological feature of PD is the appearance of aggregated α ... -synuclein (ASN), in the form of Lewy bodies (LBs) and Lewy neurites (LNs). Currently available treatments provide only symptomatic relief, without addressing the underlying pathophysiology, such as aggregation of ASN. Iron, oxidative stress and oxidized dopaminergic species have been implicated in ASN aggregation. Our approach is to develop anti-PD therapeutics that are multifunctional in nature with dopamine agonist activity along with either iron-chelation or antioxidant and ASN aggregation inhibition activities. Our aim is to develop disease modifying agents that have the ability to act on multiple targets that are relevant to pathogenesis of PD. At present, we are able to demonstrate aggregation of ASN under the following conditions: alone, dopamine,

dopamine along with hydrogen peroxide, and iron. Using silver staining, thioflavin-T (ThT) assay, atomic force microscopy (AFM) and size exclusion chromatography, we have observed a reduction of aggregation in the presence of ascorbic acid, rifampicin and lead compound. We are developing an SAR study, incorporating known ASN aggregation inhibitor moieties, into our established D2/D3 pharmacophore structure. Preliminary study indicate that presence of our lead molecule decreased the dopamine induced oligomeric ASN production. Detail characterization of the lead molecule(s) on modulation of ASN aggregation will be discussed.

Supported by National Institute of Neurological Disorders and Stroke/ National Institute of Health (NS047198, AKD).

Abstract No. 15 (Post_Doctoral_Fellow)

Title

Nifedipine prevents etoposide-induced caspase-3 activation, prenyl transferase degradation and loss in cell viability in pancreatic β ... -cells

Affiliations

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Authors

Daleep Arora PhD, Abiy Mohammed MSc, and Anjaneyulu Kowluru PhD

Abstract

Protein farnesylation and geranylgeranylation represent posttranslational modifications, where an isoprenoid tail is incorporated into the C-terminal cysteine residues of substrate proteins [e.g., small G-proteins] via a thioester linkage.

Such modifications are felt to increase the hydrophobicity of the modified proteins to facilitate their membrane association and optimal interaction with their effector proteins. Farnesyltransferase (FTase) and geranylgeranyltransferase (GGTase) catalyze incorporation of either a farnesyl [C15] or geranylgeranyl [C20] groups into substrate proteins, respectively. Ras G-proteins are farnesylated by FTases where as Rho subfamily of G-proteins are geranylgeranylated by GGTases. It is noteworthy that both FTase and GGTase share a common alpha-subunit, but variable beta-subunits.

Emerging evidence implicates novel roles for post-translational prenylation [i.e., farnesylation and geranylgeranylation] of various signaling proteins in a variety of cellular functions including hormone secretion, survival and apoptosis. In the context of cellular apoptosis, it has been shown previously that caspase-3 activation, a hallmark of mitochondrial dysregulation, promotes hydrolysis of several key cellular proteins. We report herein that exposure of insulin-secreting INS 832/13 cells or normal rat islets to etoposide leads to significant activation of caspase-3 and subsequent degradation of the common α ... -subunit of farnesyl/geranylgeranyl transferases [FTase/GGTase]. Furthermore, the above stated signaling steps were prevented by Z-DEVD-FMK, a known inhibitor of caspase-3. In addition, treatment of cell lysates with recombinant caspase-3 also caused FTase/GGTase α ... -subunit degradation. In addition, nifedipine, a calcium channel blocker, markedly attenuated etoposide-induced caspase-3 activation, FTase/GGTase α ... -subunit degradation and loss in metabolic cell viability in these cells. Based on these findings, we predict that etoposide induces loss in cell viability could be via promoting accumulation of intracellular calcium resulting in mitochondrial dysfunction, caspase-3 activation and degradation of FTase/GGTase α ... -subunit. Potential significance of these findings in the context of protein prenylation and β ... -cell survival is discussed.

Abstract No. 16 (Post_Doctoral_Fellow)

Title

Rab-geranylgeranyl transferase regulates glucose-stimulated insulin secretion from pancreatic beta cells

Affiliations

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Authors

Daleep Arora PhD, Ismail Syed PhD, Baker Machhadieh MD, Charles E. McKenna PhD, and Anjaneyulu Kowluru PhD

Abstract

A growing body of evidence implicates essential roles for small molecular weight G-proteins [e.g., Cdc42, Rac1, Arf6 and Rab3A and Rab27A] in islet β ... -cell function including glucose-stimulated insulin secretion [GSIS]. One of the known mechanisms for optimal activation of small G-proteins involves post-translational prenylation, which is mediated by farnesyltransferase [FTase] and geranylgeranyl transferases [GGTases I and II]. The FTase catalyzes incorporation of a 15-carbon farnesyl group while the GGTase mediates incorporation of a 20-carbon geranylgeranyl group into the C-terminal cysteines of G-proteins. The FTase, GGTase I and GGTase II prenylate Ras, Cdc42/Rac1, and Rab G-proteins, respectively. While considerable evidence exists on FTase/GGTase I-mediated regulation of GSIS, very little is known about GGTase II [also referred to as Rab GGTase ... RGGT] and its regulatory proteins in the cascade of events

leading to GSIS. Herein, we provide the first immunological evidence to suggest expression of α ... - and β ... -subunits of RGGT in clonal INS 832/13 β ... -cells, normal rat islets and human islets. Furthermore, Rab escort protein1 [REP1], which has been shown to be critical for prenylation of Rab G-proteins, is also expressed in these cells. Furthermore, evidence is presented to suggest that siRNA-mediated knockdown of α ... - or β ... -subunits of RGGT and REP1 markedly attenuates GSIS in INS 832/13 cells. These findings provide the first evidence in support of key roles for RGGT and its regulatory proteins in GSIS.

Abstract No. 17 (Student_Graduate)

Title

FOOT CARE AND EXERCISE BEHAVIORS/KNOWLEDGE AT A DIABETES EDUCATION & WELLNESS STUDENT-RUN CLINIC – A PILOT STUDY

Affiliations

Wayne State University

Authors

Cierra Boprie, SPT ... Ashleigh Brueck, SPT ... Alex Patterson-Tichy, SPT ... Martha Schiller, PT, DPT, MSA, C/NDT

Abstract

INTRODUCTION: Management of type II diabetes includes pharmaceutical and medical care, exercise, regular foot exams and incorporating healthy lifestyles. Previous research reports deficits in education and knowledge regarding the importance of exercise and foot care. A multidisciplinary Diabetes Education and Wellness (DEW) clinic has been developed in collaboration with Wayne State University and the SAY Detroit Family Health Care Clinic to provide education to underserved women with type II diabetes. The purpose of this

study is to determine the short term effects of a standardized educational program regarding exercise and foot care on knowledge and behavior changes in an urban under/uninsured diabetic population. METHODS: This was a prospective study with a pre/post design and patients served as their own control. Eleven participants with type II diabetes were recruited from the DEW Clinic. Participants attended the clinic for a total of four visits. All participants received diabetes foot care, exercise education and a home program provided by physical therapy student volunteers and physical therapists. All participants completed The Summary of Diabetes Self-care Activities Measure (SDCA) and The Spoken Knowledge in Low Literacy in Diabetes Scale (SKILLD) at visit one and four. Outcomes were analyzed pre and post intervention. Descriptive statistics were analyzed using SPSS. RESULTS: Data was analyzed for subjects, all African American women with a mean age of 50.50 (SD 4.5). Subjects reported that foot examinations and exercise were important for controlling/preventing complications from diabetes, with a mean of 4.33 (SD1.6) and 4.83 (SD .41) respectively on a scale of 0 to 5. At visit 1, subjects reported participating in foot care activities (foot and shoe inspection) on average 3.75 days/week. Of those that completed all 4 visits, the average increased to 7 days/week. At visit 1, subjects reported participating in physical activity or exercise on average for 2.83 days/week. Of those that completed all 4 visits, the average increased to 7.0 days/week. When responding to the specific questions on foot care and exercise on the SKILLD tool, the subjects pre-intervention answered 48% of the questions correctly and 58 % post-intervention on visit 1. Of those that completed all 4 visits, subjects answered 83% correctly. DISCUSSION: The majority of participants indicated that exercise and foot exams were important with controlling and preventing complications from diabetes but their frequency of behavior demonstrating this at visit one were not at the recommended levels. Preliminary data are encouraging with trends demonstrating an improvement in short term behavior changes with respect to exercise and foot care despite the small sample size. CONCLUSION: Change in frequency in

behaviors relating to foot care and exercise were made by subjects participating at the DEW clinic. This is a positive step in diabetes management and a benefit of physical therapy intervention at the DEW clinic.

ACKNOWLEDGMENTS: A special gratitude to the SAY Detroit Family Health Clinic, volunteers and donors for making this project possible.

Abstract No. 18 (Student_Graduate)

Title

RELATIONSHIP BETWEEN LOWER EXTREMITY STRENGTH AND BALANCE IN 6 AND 8 YEAR OLD CHILDREN

Affiliations

Authors

Duhaime KM, MacIntyre EM, Nycek KE, Carlson CL, Talley, SA ... Physical Therapy Program, Wayne State University, Detroit, MI

Abstract

INTRODUCTION: Activity limitations and participation restrictions have been observed in children with conditions resulting in LE muscle weakness. Normative data on muscle strength and balance in children is needed for comparative purposes. Understanding the relationship between muscle strength and balance in children may help physical therapists identify interventions to improve function in children with strength and balance impairments. Lower extremity (LE) muscle strength has been shown to be significantly correlated with motor function in healthy preschool children. While strength and balance have been studied independently, there are no studies examining the relationship between LE muscle force and balance in young children. The purpose of this study was to examine the relationship between LE muscle strength and postural sway in 6 and 8 year old (YO) children. METHODS: Forty

typically developing children were recruited from a suburban public school. Twenty participants (50% female) were 6 YO and twenty (50% female) were 8 YO. Height and weight were measured and dominant leg and ethnicity were recorded. Children with known neurological or other conditions which would prevent participation were excluded from the study. The strength of 8 LE muscle groups were measured in the preferred leg using a Lafayette hand-held dynamometer using a "make" test. Standardized positions and stabilization were used. The mean force in kg was computed from 3 trials each for ankle dorsiflexion, plantarflexion, inversion, eversion, knee extension, flexion, and hip abduction, adduction. Postural sway was measured using a portable Balance Master System. Four conditions were tested: bipedal stance with eyes open and eyes closed and tandem stance with eyes open and eyes closed. Center of pressure displacement was measured during three 10-second trials in each position and the mean was recorded in degrees per second. Descriptive statistics were used for demographic information. T-test for independent samples was used to compare means between the age groups. Pearson's correlation was used to examine the relationship between strength and postural sway. Alpha was set at 0.05. RESULTS: LE strength was significantly stronger in the 8 YOs for all muscle groups except hip abduction, increasing from 14.7% - 25.4%. Postural sway decreased in all conditions in the 8 YOs, but only significantly for the bipedal stance - eyes closed condition. When adjusted for height, postural sway also decreased significantly in the two tandem stance conditions. There was only one significant correlation between muscle strength and postural sway: ankle eversion and tandem stance-eyes closed ($r=-.38$). CONCLUSIONS: Normative data for LE muscle strength and postural sway is provided for typically developing 6 and 8 YO children. LE muscle strength was significantly stronger in the 8 YOs compared to the 6 YOs for all but one movement. The rank order of muscles producing the greatest to the least force did not change. Knee extension consistently produced the greatest force while ankle inversion generated the smallest force in both groups. Postural sway decreased significantly in

the 8 year old group in the bipedal stance-eyes closed condition.

Abstract No. 19 (Student Graduate)

Title

Structure-activity-relationship study of N6-(2-(4-(1H-indol-5-yl)piperazin-1-yl)ethyl)-N6-propyl-4,5,6,7-tetrahydrobenzo[d]thiazole-2,6-diamine analogues: Development of highly selective D3 dopamine receptor agonists along with a highly potent D2/D3 agonist and their pharmacological characterization"

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Authors

- (1)Mark Johnson, (2)Tamara Antonio, (2)(3)Maarten E. A. Reith and (1)Aloke K. Dutta

Abstract

In our effort to develop multifunctional, therapeutic agents against Parkinson's disease (PD), we have carried out a structure-activity-relationship study based on our previously reported hybrid, molecular template targeting D2/D3 receptors. Binding assays were carried out with HEK-293 cells expressing either D2L or D3 receptor. Competitive binding with [3H]spiroperidol was used to evaluate inhibition constants (K_i) of test compounds. Functional activity of selected compounds in stimulating [35S]GTP γ ... S binding was assessed in CHO cells expressing human D2L and D3 receptors.

SAR results demonstrated development of highly selective compounds for D3 receptor ((-)-40 ... Ki D3 = 1.84 nM, D2/D3 = 583.2 ... (-)-45 ... Ki D3 = 1.09 nM, D2/D3 = 827.5 and (-)-46 ... Ki D3 = 1.40 nM, D2/D3 = 736). Functional data indicated high selectivity of (-)-40 (EC50 D2 = 114 nM, D3 = 0.26 nM, D2/D3 = 438) and full agonist activity at the D3 receptor. In addition, highly potent, non-selective, D2/D3 agonist, (-)-19 (EC50 D2 = 2.96 nM, D3 = 1.26 nM), was also developed. Radical quenching study indicated potent antioxidant activity in the selected target compounds. Lead compounds were evaluated using an in vivo PD animal model. Future studies will explore the potential use of these compounds as a neuroprotective therapy for PD.

Abstract No. 20 ()

Title

Evaluation of Nephrotoxicity in Patients Receiving \geq ... 3 grams/day of Vancomycin

Affiliations

Wayne State University and St. John Hospital and Medical Center

Authors

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Abstract

Purpose: To evaluate nephrotoxicity in patients receiving vancomycin \geq ... 3 grams/day compared to < 3grams/day.

Methods: We conducted a retrospective analysis of 240 patients admitted to a community teaching institution who received vancomycin. We compared incidence of nephrotoxicity

defined as an increase in SCr > 0.5 mg/dL or > 50% increase from baseline, with vancomycin doses \geq ... 3 g/day and < 3 g/day. Our secondary endpoint was to identify risk factors associated with nephrotoxicity in these patients. Patients greater than 18 years of age who received vancomycin for more than 48 hours were included. Patients with a CrCl <30 ml/min or undergoing dialysis were excluded. Nominal variables were analyzed using Chi-square. Factors found significant ($p < 0.10$) in the univariate analysis were included in a stepwise multivariate logistic regression.

Results: A total of 26 cases of nephrotoxicity (10.8%) occurred. Nephrotoxicity occurred in 9.1% and 14.7% of patients that received \geq ... 3grams/day and <3 grams/day respectively. Patients in the \geq ... 3 grams/day group had a mean initial and maximum trough of 15mcg/mL \pm 7.1mcg/mL and 17.8mcg/mL \pm 7.2mcg/mL respectively, compared to 13mcg/mL \pm 6.0mcg/mL and 15.1mcg/mL \pm 7.5mcg/mL respectively, in the <3gram/day. The median duration of vancomycin therapy was 5 days in both groups. A Charlson Weight Index of Comorbidity (CWIC) of \geq ... 5 occurred in 10/165 of patients receiving \geq ... 3grams/day and 7/75 patients receiving <3 gram/day. Mean creatinine clearance (CrCl) was 96mL/min in the \geq ... 3grams/day and 61mL/min in <3gram/day group. Significant factors identified in the univariate analysis included vancomycin \geq ... 3grams/day, skin and soft tissue infections, maximum trough > 20mcg/mL, CrCl < 85ml/min, intensive care unit (ICU) residence, length of stay (LOS) > 14 days, CWIC \geq ... 5, age > 55, and nephrotoxins. Factors that remained significant in the multivariate analysis included ICU residence OR = 3.65 (95% CI 1.45 – 9.20), CWIC \geq ... 5 OR=3.5 (95% CI 1.01 – 12.13), and LOS > 14 days OR=3.23 (95% CI 1.27 – 8.23). Vancomycin doses \geq ... 3grams/day were not associated with nephrotoxicity OR 0.52 (95% CI 0.21 – 1.30).

Conclusion: We found ICU residence, CWIC \geq ... 5, and LOS > 14 days were significant predictors of nephrotoxicity. Vancomycin doses \geq ... 3grams/day were not a significant predictor

of nephrotoxicity. Future studies need to be conducted to elucidate this association.

Abstract No. 21 ()

Title

Approach towards development of multifunctional drugs as an effective strategy for treatment of Parkinson's disease.

Affiliations

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Authors

Soumava Santra,¹ Liping Xu,¹ Mark Johnson,¹ Tamara Antonio,² Maarten E. A. Reith,² Alope K. Dutta^{1*}

Abstract

Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by degeneration of the nigrostriatal dopaminergic pathway. The etiology of PD is not fully understood. Both oxidative stress and mitochondrial dysfunction have been strongly implicated in cell death. The role of iron in the pathogenesis of Parkinson's disease (PD) has been implicated strongly due to generation of oxidative stress leading to dopamine cell death. In addition, α ... -synuclein, a presynaptic protein involved in fibrilization, has been implicated in the pathogenesis of PD. A recent report demonstrated in cultured, human dopaminergic neurons that accumulation of α ... -synuclein induces apoptosis in the presence of DA and reactive oxygen species. It is increasingly evident that for a complex disease such as PD, a drug aimed at one target site will only partially address the therapeutic need of the disease. Thus, it is hypothesized that multifunctional drugs, having multiple pharmacological activities, will be more

effective in the case of PD. In our overall goal to develop bifunctional/multifunctional drugs as neuroprotective treatment agents for PD, we designed dopamine D2/D3 agonist molecules with potent antioxidant activity as well as some such agonists with a capacity to bind to iron. Such molecules should not only address symptomatic aspect of the disease by normalizing motor dysfunction but also at the same time should slow down or stop the process of degeneration. New molecules were subjected to binding assays with HEK-293 cells expressing either D2 or D3 receptors with tritiated spiperone to evaluate inhibition constants (K_i). The lead molecules exhibited high affinity for the both D2 and D3 receptors. Functional activity of selected compounds was carried out in GTP γ ... S binding assay. SAR results identified compounds with potent agonists activity at both D2 and D3 receptors (EC_{50} (GTP γ ... S) ... D2 = 27 and 2 nM and D3 = 4.98 and 1.26 nM etc., respectively). The lead compounds were efficacious in animal models of PD. In vivo and in vitro neuroprotection assays indicated potent neuroprotection properties of these molecules. Detailed discussion on these experiments will be presented.

Abstract No. 22 (Faculty)

Title

Pharmacist Roles During the Transitions of Care for Heart Failure Patients

Affiliations

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Authors

Melissa Lipari, PharmD ^{1,2}, Jessica L. Jones, PharmD ¹, Lynette Moser, PharmD ^{1,2}

Abstract

Background: High rehospitalization rates in patients with heart failure (HF) have been attributed to challenges during transitions of care and medication nonadherence. Patients with HF often have multiple coexisting conditions that require care from different practitioners with resulting highly complex and costly drug regimens. During care transitions patients are at risk for medical errors, service duplication, inappropriate care, and mismanagement of critical elements of the care plan. Upon both hospital admission and discharge, patients may be susceptible to prescription errors, including the unintentional discontinuation of medications, therapeutic duplication, and inappropriate dosing of medications. Our institution recently implemented an inpatient Pharmacist provided Medication History service and a Pharmacy Medication Adherence Clinic (MAC) to aid in these transitions.

Methods and Results: Pharmacist interventions in both services were documented within the electronic medical record (EMR) and data was retrospectively extracted and reported descriptively. For the medication history service, patients were included if they were identified as heart failure patients via an electronic inpatient HF list and were able to communicate. The pharmacists spoke to the patient and then corroborated the medication list with the outpatient pharmacy to generate an accurate medication history, with appropriate documentation in EMR. Pharmacists then identified discrepancies and drug related problems (DRPs) between the inpatient and home medications and interacted with prescribers to resolve these problems. One hundred two patients received a medication history from pharmacy. The pharmacists corrected 5.4 errors per history to the EMR documented medications and documented 233 DRPs that required clinical intervention. The 30-day rehospitalisation rate for patients included in this study was reduced from 27.4% to 25.5%, but still above the national average of 24.8%.

The same heart failure database was used to identify inpatients with heart failure who had

been hospitalized twice in the previous year and therefore at high risk for rehospitalization. These patients were seen twice after discharge in the MAC. The visit included a complete assessment and education about their medications, sodium restriction, self-monitoring, and activity. EMR documentation was retrospectively reviewed to identify drug or disease related problems (DRPs) and subsequent pharmacist interventions. Thirteen patients have been seen in the clinic. The pharmacist identified 83 DRPs (average of 5.2 / visit) and 39 reasons for non-adherence. The pharmacist provided 223 interventions (average of 14 / visit), including patient education, removal or adherence barriers, and recommendations to prescribers.

Conclusions: Pharmacists are well suited to make effective interventions and improve patient safety during the vulnerable transition of care period.

Abstract No. 23 (Faculty)

Title

MUSCLE STRENGTH CHANGES RECORDED USING DYNAMOMETRY DURING ROBOT ASSISTED GAIT TRAINING.

Affiliations

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Authors

Sujay Galen, PhD ... Celia Clarke¹ PhD ... David Allan² FRCS ... Bernard Conway¹ PhD

Abstract

Background: The Lokomat (Hocoma) is a commercially available robot assisted BWSTT.

Although previous studies have shown functional improvements in gait following Lokomat training in ISCI, the strength changes in lower limb muscles following BWSTT has received little attention. The aim of this study was to record changes in muscle strength in key lower limb muscle groups in acute and chronic ISCI patients undergoing daily Lokomat training.

Methods: Eighteen patients (acute = 13, chronic = 5) with ISCI participated in this study (Age range: 26-63 years, mean = 49.33 + 11.04 years). Each patient underwent a six week Lokomat training program consisting of a daily target of 1 hour of BWSTT. In this study we used the Lokomat's ability to measure isometric hip and knee joint moment in order to chart weekly changes in the maximal voluntary strength changes in the flexor and extensor muscles groups of those joints. Isometric measurements were made prior to the start of Lokomat training and during the middle of each training week. Patients were positioned in an upright standing posture within the Lokomat and instructed to make maximal efforts of flexor and extensor muscle groups of the hip and knee against a fixed orthosis. The best of three attempts of each exertion was taken as an estimate of the maximal voluntary strength. Rest periods between each exertion were given in order to avoid fatigue.

Results: For all muscle groups tested there was a significant increase in the maximal strength recorded in the acute patient group ($p < 0.05$). The time course of the changes reveals that in responding patients who demonstrate functional improvements in gait that there is clear evidence of strength increases in the hip and knee musculature within 3 weeks of training onset. This increase in strength continues to rise throughout the training program but not in a simple linear fashion. In the chronic patient group strength changes were also seen but were of a lesser magnitude than those seen in the acute group.

Discussion/Conclusions: This study objectively measured the changes in muscle strength following robot assisted BWSTT. For patients receiving Lokomat rehabilitation the observation that increased hip and knee moments in responding patients can be seen by week 3 is

indicative of treatment efficacy. However, in patients lacking a positive increase in strength by week 3 may denote that the patient is receiving no physiological benefit from the robot assisted BWSTT. Incorporating, regular dynamometry may therefore assist in revising treatment planning for patients who are considered for Lokomat or other forms of BWSTT.

Abstract No. 24 (Student_Graduate)

Title

Intra-rater and Inter-rater Reliability of Timed Cervical Flexor and Extensor Endurance Tests

Affiliations

Wayne State University Physical Therapy

Authors

Elana Bodzin, SPT, Kristen Evey, SPT, Amanda Rowley, SPT, Kim Dunleavy, Ph.D, PT, OCS

Abstract

Objective: The purpose of this study is to determine if timed cervical flexion and extension endurance tests show sufficient same day intra- and inter-rater reliability as well as inter-session test-retest reliability for use in clinical or research settings without increasing pain in normal subjects.

Methods: Twenty subjects with neck pain $< 3/10$ on Visual Analogue Scale (VAS) performed three trials of cervical flexion and extension endurance tests. Intra-rater reliability was determined using the last 2 measurements. Two raters tested cervical flexion endurance using a timed modified version of the Cervical Flexion Test using a biofeedback cuff and timed cervical positions against gravity using the Cervical Range of Motion device and a laser device. Three trials were conducted in two sessions with reliability calculated from the last 2 trials. Reliability was tested using Intra-class

correlation coefficients. Pain was assessed using the Neck Disability Index (NDI) and VAS before and after the tests as well as at 24 and 48 hours.

Results: Intra-rater reliability for session A flexion endurance tests was moderate (ICC3,1 = 0.54) and good in session (ICC3,1 = 0.93). Intra-rater reliability for session A extension endurance tests was moderate (ICC3,1 = 0.54) and poor to moderate for session B (ICC3,1 = 0.47). Inter-rater reliability was excellent for both neck flexion and extension measurements for both sessions (ICC2,1 = 1.00). Same day test-retest between session reliability was good for flexion tests (ICC3,1 = 0.70) and fair to moderate for extension tests (ICC3,1 = 0.70). VAS pain scores and NDI did not increase significantly.

Conclusions: This study showed moderate to good intra-rater reliability for cervical flexion and fair to moderate intra-rater reliability for extension submaximal muscle endurance tests in normal subjects. As the measurement consistency between testers was very uniform, participant performance variability is likely to have contributed to moderate intra-rater reliability. While flexion test consistency improved with practice from session A to B, extension test consistency diminished possibly due to fatigue or difficulties obtaining a consistent anti-gravity position. The tests did not result in pain after testing or in the next 2 days suggesting that these tests are more suitable for patients than resisted tests. The use of a modified cervical flexion endurance test is sufficiently reliable using the means of the last 2 of 3 measurements, while the extension endurance test reliability was only moderate and is not recommended without adjustments to address proprioceptive challenges in a midrange position. Further research is needed to test the reliability of the modified flexion test for individuals with neck pain, while the timed extension endurance test used for this study is not sufficiently reliable to provide repeatable results with normal subjects. Modifications are needed to accommodate for proprioceptive challenges.

Abstract No. 25 (Student_Graduate)

Title

Lyophilization of biodegradable DEAPA-PVA-PLGA for siRNA delivery

Affiliations

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Authors

Maha Elsayed¹, B.Sc Pharmacy
Na Hyung Kim¹, Ph.D
Venkatarreddy Nadithe¹, Ph.D
Olivia Merkel¹, Ph.D

Abstract

Objective:

DEAPA-PVA-(72)-PLGA is a biodegradable non-viral vector ... however it has a rapid degradation rate under physiological conditions [1]. Our main objective is to enhance the long term stability and shelf life of the nanoparticles which are intended for the delivery of siRNA via pulmonary route. This can be achieved by the lyophilization process to form a dry inhalable powder of nanoparticles.

Methods

Cytotoxicity of DEAPA-PVA-(72)-PLGA was evaluated by MTT assay in H1299 non-small cell lung cancer cells. Nanoparticles were formed according to Nguyen et al [1] by the solvent displacement method with N/P ratio 10. Size and zeta potential were evaluated using dynamic light scattering (DLS). Size and morphology were confirmed with SEM and TEM. The lyophilization process was performed by using a freeze dryer for two days after adding 10% glucose, 5% sucrose and trehalose solutions as lyoprotectants. Sizes were then measured for the dried product after reconstitution in water.

Results

DEAPA-PVA-(72)-PLGA was found to be non-

toxic in concentrations less than 0.01-0.03 mg/ml. The nanoparticles were 217 nm in size. Zetapotential was +54.77 mV, and polydispersity was 0.055. SEM showed spherical particles and confirmed approximately the same size. Reconstituted formulations of DEAPA-PVA-(72)-PLGA nanoparticles showed sizes of 884 nm with glucose solution, 792.8 nm with sucrose solution, and 1123.8 nm with the trehalose solution.

Conclusion:

To avoid the instability of the biodegradable polymer DEAPA-PVA-(72)-PLGA, we used lyophilisation to produce a dry ready to use nanoparticle formulation. We expect this polymer to combine the properties of biodegradability and long stability. The lyophilized product still needs to be optimized in terms of the size. Additionally, other experiments will be conducted in the future to test the gene knock down efficiency for the dried product.

1. Nguyen, J., et al., Fast degrading polyesters as siRNA nano-carriers for pulmonary gene therapy. *Journal of Controlled Release*, 2008. 132(3): p. 243-251.

Abstract No. 26 (Student_Graduate)

Title

Glucotoxicity induces lamin-B degradation in the pancreatic beta-cell

Affiliations

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Authors

Khadija Syeda, Abiy Mohammed and Anjan Kowluru-PhD

Abstract

Lamins are nuclear membrane proteins that are vitally important for the structural integrity of the nucleus and the overall functions of the cell. Nuclear lamins form the nuclear lamina on the interior of the nuclear envelope. Their major functions are regulation of various nuclear processes, including DNA replication, transcription and chromatin organization. It has been reported that degradation of lamins occurs by a caspase dependent mechanism causing nuclear collapse which leads to cell death. Previous results from our laboratory indicated that IL-1 β ... treatment causes an increase in lamin B degradation by caspases. Herein, we investigated potential effects of glucotoxicity on lamin B degradation. Our findings suggested that incubation of insulin-secreting INS 832/13 cells under glucotoxic conditions [20mM for 12-48 hrs] results in the degradation of lamin B. We also noticed a significant increase in the activation of caspase-3 under these conditions. Furthermore, a marked increase in the cleavage of the alpha subunit of prenyltransferase was seen under glucotoxic conditions. Together, our data suggest that glucotoxic conditions induce caspase-3 activation culminating in the cleavage of its substrate proteins including prenyltransferase and lamin B. Studies are in progress to determine if reduction in the requisite prenylation of lamin B as a result of prenyltransferase degradation under glucotoxic conditions further

Abstract No. 27 (Student_Graduate)

Title

Effects of fluoroquinolone antimicrobial stewardship education on resistance rates

Affiliations

Oakwood Hospital and Medical Center
Wayne State University

Authors

Lama Hsaiky, PharmD.

Ray Cha, PharmD.

Teresa Breslin, Doctor of Pharmacy Candidate,
2013

Norma Peters, Doctor of Pharmacy Candidate,
2013

Abstract

Background: Frequent use of broad spectrum antibiotics plays a significant role in the development of resistant strains of bacteria. Fluoroquinolones (FQ) have become the most commonly prescribed class of antibiotics in the US with an estimated increase of 15 million FQ prescriptions between 1995 and 2002. Fluoroquinolones are indicated for the treatment of many infections, such as pneumonia, urinary tract infections and intra-abdominal infections. With the increase in inappropriate prescribing, there has been a rapid development of resistance of key pathogens such as *P.aeruginosa* and *Klebsiella* spp. The aim of this study is to determine the impact of a pharmacy directed antimicrobial stewardship program on the appropriate use of fluoroquinolones and impact on nosocomial pathogen resistance rates and fluoroquinolone prescribing patterns.

Objective: Evaluate the changes in fluoroquinolone prescribing patterns and resistance rates after implementation of antimicrobial stewardship monitoring and education programs regarding the use of fluoroquinolones.

Methods: Prior to initiation, this study will be submitted to the Institutional Review Board. Upon approval, a retrospective analysis will be performed on the number of interventions completed, the impact of these interventions on fluoroquinolone prescribing and the effect of the antimicrobial stewardship program on resistance patterns. Data collected will include total number of pharmacist interventions, number of fluoroquinolone orders, percent of fluoroquinolone discontinuation by day 3 and percent change in resistance rates after

implementation of this program.

Results: The goal of the antimicrobial stewardship program at our institution was to decrease inappropriate prescribing of all antibiotics. One of the focuses of our program was to monitor daily antibiotics prescribed. The purpose of this study was to evaluate the effects of this program on fluoroquinolones. In September of 2010, prescribers were alerted of the noticeable overprescribing of fluoroquinolones in the institution via electronic newsletters, mail and facsimile. Informational materials were distributed to prescribers and in physician offices to guide the proper prescribing of empiric antimicrobial therapy. In early October 2010, evaluation for appropriateness of all fluoroquinolone orders was implemented. This included daily monitoring of patients on fluoroquinolones to evaluate indication for use and appropriate duration and dosing. Upon evaluation, the prescribers were contacted via telephone or communication notes in patient charts to recommend de-escalation or discontinuation. The pharmacists' daily monitoring was effective in reducing the overall number of fluoroquinolones prescribed by 50% in the first month and was maintained thereafter. During this time, the percent of fluoroquinolone orders discontinued by day 3 increased by up to 30%. Additionally, the overall reduction in fluoroquinolone use contributed to a 7% decrease in the incidence of extended-spectrum beta-lactamase (ESBL) producing *Klebsiella pneumoniae* and a 9% increase in *Pseudomonas aeruginosa* susceptibility to fluoroquinolones.

Conclusion: The implementation of antimicrobial stewardship monitoring and education programs regarding the use of fluoroquinolones has a positive impact on fluoroquinolone prescribing patterns and resistance rates.

Abstract No. 28 (Student_Graduate)

Title

Nephrotoxicity Risk and the Use of Concomitant Vancomycin and Piperacillin/Tazobactam

Affiliations

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Wayne State University

Authors

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Ray Cha, PharmD.
Norma Peters, Doctor of Pharmacy Candidate,
2013

Abstract

Background: The combination of vancomycin and piperacillin/tazobactam is a regimen frequently used as empiric therapy for the treatment of infections. Vancomycin has been shown to cause nephrotoxicity, however there is little evidence to prove whether or not the combination of vancomycin and piperacillin/tazobactam has a synergistic effect on this nephrotoxicity. The question of potential nephrotoxicity due to the combination of these medications has been proposed in recent literature. The aim of this study is to determine the incidence of nephrotoxicity in those being treated with both vancomycin and piperacillin/tazobactam simultaneously.

Objective: Evaluate the incidence of nephrotoxicity in patients receiving vancomycin and piperacillin/tazobactam concomitantly and to determine any factors affecting the risk of nephrotoxicity.

Methods: Prior to initiation, this study will be submitted to the Institutional Review Board. Upon approval a retrospective analysis will be performed on patients from January 2009-present treated with both vancomycin and piperacillin/tazobactam for at least 24 hours.

Data collected from a retrospective chart review, through the use of a data collection sheet, includes baseline demographic data, serum creatinine at initiation and conclusion, baseline albumin, APACHE II scores, concomitant disease states, indication for antibiotic use, unit of stay, duration and dose of both vancomycin and piperacillin/tazobactam, vancomycin levels, number of concomitant nephrotoxic agents used and need for dialysis. The primary outcome measured will be nephrotoxicity defined by RIFLE criteria. A secondary outcome will be hospital length of stay. All data will be de-identified.

Abstract No. 29 (Post_Doctoral_Fellow)

Title

Functional studies of of N5-Carboxyaminoimidazole Ribonucleotide Synthetase by Site-Directed Mutagenesis of Critical Active Site Residues

Affiliations

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Authors

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Abstract

The increasing number of drug-resistant bacterial and fungal infections is a serious threat to the healthcare community. The enzyme N5-carboxyaminoimidazole ribonucleotide synthetase (N5-CAIR synthetase) is an attractive target in antimicrobial drug design.¹ This enzyme, found in de novo purine biosynthesis, is required by bacteria, yeast, and fungi, but is

absent in humans. To aid our drug discovery efforts and to elucidate the mechanism of the enzyme, we conducted site-directed mutagenesis of active site residues (H273, R271, R155 K353, Y152, E73 and D153). These residues play a critical role in substrate binding and catalysis. The mutated enzymes were analyzed by steady-state kinetics for the complete forward reaction as well as the partial forward reaction. The mutants H273A and R271K allowed us to discover cooperative substrate binding for both the complete and partial forward reactions. To aid in our understanding of the functional role played by residues, we aligned the crystal structures of biotin carboxylase and N5-CAIR synthetase. The results of these studies will be presented.

Abstract No. 30 (Faculty)

Title

Intra-rater reliability and validity of Upper and Lower Cervical Position measurements using the CROM device

Affiliations

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Authors

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Abstract

INTRODUCTION: Postural re-education is used frequently for clinical management neck pain particularly for individuals with seated

occupations. There is a need for valid and reliable measurement options for outcome evaluation of cervical posture. Although the reliability of the cervical range of motion device (CROM) for forward head position (FHP) is good, criterion validity has not been reported. In addition, the reliability and validity of upper cervical flexion/extension angle (UCA) in naturally adopted postures have not been reported. The purpose of this study was to establish the following for FHP and UCA measurements using the CROM and Optotrak systems: 1) test-retest reliability 2) criterion validity 3) standard error of measurement (SEM) and minimal detectable change at the 95% confidence level (MDC95), and 4) differences in FHP and UCA between habitual (HAB) and erect (ER) postures. METHODS: A within-subjects single session design was used. FHP and UCA were measured using the CROM followed by Optotrak measurement in habitual (HAB) and erect postures (ER) in 16 healthy young adults. RESULTS: Test-retest reliability of CROM FHP was good in both postures (ICC 3,1 = 0.82 HAB ... 0.87 ER), and excellent for UCA in both postures (ICC 3,1 = 0.90 HAB ... 0.97 ER). LOA of FHP was -1.93 to 4.88 cm for HAB, -2.42 to 4.12 cm for ER posture. LOA for UCA was -6.5 to 3.1 deg in HAB and -7.2 to 0.2 deg for ER posture. SEM for FHP was larger for the CROM (1cm) compared to OP (0.3 cm). UCA SEM was low with both measurement systems (1-2 deg). CROM FHP MDC95 in both postures was low and feasible (2.9 cm, HAB ... 2.4 cm). FHP was significantly less in ER compared to HAB postures CROM (1.2 cm) and Optotrak (0.56cm) distances ($p < 0.001$). ER posture resulted in significantly more UCA extension measured with the Optotrak (2.78 degrees ... $p < 0.001$), which was not reflected by the CROM (1 degree ... $p > 0.05$). DISCUSSION: Reliability of the FHP and UCA in both postures were good (CROM) and excellent (Optotrak) supporting repeatability without standardization of UCA. Criterion validity of the CROM FHP and UCA measurements compared to Optotrak measurements showed trends towards systematic bias and bias related to the degree of angular tilt. Factors which may have contributed to differences in measurements are angular tilt of

the FHP of the CROM with changes in UCA, and large measurement increments. However, error was small and MDC95 was feasible for both measurements. **CONCLUSIONS:** Test-retest reliability of both FHP and UCA were good in both postures. LOA were less than desired to be able to regard the CROM as interchangeable for sophisticated optoelectronic measurement and some bias was evident. There are limitations in using the CROM for measurement of FHP related to angular changes in UCA. Small changes in UCA may not be reflected by the CROM.

Abstract No. 31 (Post_Doctoral_Fellow)

Title

Type II collagen induces peripheral tolerance in BALB/c mice via the generation of CD8+ T regulatory cells

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Authors

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Abstract

Antigens introduced into the anterior chamber (AC) of the eye induce a potent form of antigen-specific peripheral immune tolerance termed AC-associated immune deviation (ACAID), which prevents inflammatory immune responses and is characterized by impaired delayed-type

hypersensitivity (DTH) responses. Type-II collagen (CII) is a fibrillar protein expressed exclusively in cartilage tissues. Although of its clinical relevance to Rheumatoid arthritis, aging, and osteoarthritis, there have been no studies to date to test if CII has the ability to induce ACAID. We hypothesized that ACAID could be generated via AC injection of CII in BALB/c mice. Using a DTH assay, the hypothesis was supported and led to another hypothesis that CII is capable of inducing specific immune tolerance via CD8+ T regulatory cells (Tregs). Thus, we performed functional local adoptive transfer (LAT) assays to examine the regulatory roles of spleen cells, T cells, and CD8+ T cells in the specific immune regulation induced by CII injection into the AC. Results indicated that CII induced ACAID when injected into the AC. Spleen cells of mice injected with CII in the AC significantly suppressed DTH responses. The T cell compartment of the spleen was capable of expressing this suppression. CD8+ Tregs could solely express this CII-driven suppression and even exerted more noticeable suppression than spleen cells or splenic T cells. This study suggests a crucial role for CD8+ Tregs in mediating CII-driven ACAID-mediated immune tolerance. This could have therapeutic implications in Rheumatoid arthritis, aging, osteoarthritis, and other diseases in which CII is involved.

Abstract No. 32 (Post_Doctoral_Fellow)

Title

Further structure activity relationship studies of 4-(((3S,6S)-6-benzhydryltetrahydro-2H-pyran-3-yl)amino)methylphenol and its analogs: Identification of novel triple uptake inhibitors as new generation antidepressants

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Authors

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Abstract

Major depression disorder is significant health problem with 10-20% of all adults suffering from this disease. Monoamine therapies have so far been the most successful approach for treating depression. Although dopaminergic inhibition has been strongly associated with depression evidenced by preclinical and clinical studies, currently available treatment involves inhibition of serotonergic and noradrenergic system but not dopaminergic neurotransmission. Recently, triple reuptake inhibitors (TUI), which inhibits uptake of all three neurotransmitters, have recently been implicated in new generation of potent antidepressants. Preclinical studies indicate that a drug inhibiting the uptake of all three of these neurotransmitters could produce a more rapid onset of action and should possess greater efficacy compared to traditional antidepressants and also address anhedonia due to additional dopaminergic activity. In our ongoing SAR studies to discover new molecules for development of novel TUIs, we have designed and synthesized several asymmetric di- and tri-substituted pyran derivatives. Uptake inhibition studies with all three monoamine transporters indicated variety of activities depending upon the nature of substitutions either on the pyran ring or on the N-benzyl moiety. SAR studies indicate the compound D-485 showed triple reuptake inhibitory (TUI) activity profile, as these molecules exhibited potent uptake inhibition for all the monoamine transporters (K_i of 234.0 nM, 2.68 nM, and 33.6 nM for DAT, SERT, and NET respectively). Synthesis and SAR studies will be presented. This work is supported by National Institute of Mental Health/ National Institute of Health MH084888 (AKD).

Abstract No. 33 (Student_Graduate)

Title

Phosphorylation of STAT3 is Associated with pAKT Recovery in Gefitinib Treated Lung Cancer Cells

Affiliations

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Authors

Kai Wu, Yongju Lu, Qingshan Chang, Qiu Ping, Bailing Chen, Fei Chen

Abstract

Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitors (TKIs), including gefitinib and erlotinib, are effective drugs for a subset of non-small cell lung cancer. Gefitinib binds to the tyrosine kinase domain of EGFR and hence inactivates its downstream prosurvival signaling pathways, including PI3k/Akt and MAPK pathways. However, most patients received gefitinib eventually developed resistance to this drug. In this study, we demonstrated that in gefitinib-treated A549 cells (human lung cancer cell line), Akt activation undergoes a time-dependent recovery following an initial inhibition by gefitinib. Since constant activation of Akt has been associated with treatment failure of gefitinib in lung cancer cells, exploring the mechanisms that lead to Akt restoration should provide new insights into the drug resistance and therapeutic efficacy. For that purpose, alterations in Akt activation and other signaling pathways, including MAPK and STAT3, involved in EGFR-mediated cellular responses were determined in A549 cells treated with gefitinib. Among them, we found that activation of STAT3 was inhibited in the cells without gefitinib treatment. Gefitinib treatment inhibited EGFR phosphorylation on tyrosine 1086 (Y1086), which leads to STAT3 activation. Additional studies showed that interruption of the STAT3 signaling by STAT3 inhibitor

prevented fast recovery of Akt activation and enhanced cell death in the gefitinib-treated cells. Taken together, these data suggest that activation of STAT3 is an intrinsic mechanism of drug resistance in response to EGFR inhibitors. Combinational targeting on both EGFR and STAT3 may enhance the efficacy of gefitinib or other TKIs on lung cancer.

Abstract No. 34 (Student_Graduate)

Title

The Prevalence of Anterior Pelvic Tilt in the Prosthetic Wearing Lower-Limb Amputee

Affiliations

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Authors

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Aimee Fullerton, SPT
Shannon Lucas, SPT
Kristina Reid, P.T., M.S., C/NDT

Abstract

Background and Purpose: Past research is limited in regards to anterior pelvic tilt (APT) prevalence in the amputee population. The purpose of this study was to examine the prevalence of APT in unilateral transtibial and transfemoral amputees and to determine differences in APT between transtibial and transfemoral amputees.

Methods: 12 participants were recruited from Wright & Fillipis Warren location who were a unilateral transtibial or transfemoral amputee, utilized a definitive prosthesis, and able to stand without an assistive device. Data was collected through the use of a brief demographic and health history form, Prosthesis Evaluation

Questionnaire (PEQ), Oswestry Disability Index (ODI), PALpation Meter (PALM), and Thomas Test. Participants were randomly assigned to a sequence of four conditions in which their anterior pelvic tilt was measured via the PALM bilaterally 3 times after each condition. These conditions included: 1) standing comfortably with their arms crossed in front of their chest (starting position), 2) performing sit to stand sequences 2 times returning to starting position, 3) walking 10 feet and returning to the starting position, and 4) marching in place 20 times and returning to the starting position. Hip flexor flexibility was taken 3 times bilaterally using a goniometer and Thomas Test protocol.

Results: Descriptive statistics revealed an average of 8.89 degrees of APT on the sound side and 8.48 degrees of APT on the amputee side of our subjects. Paired Samples t-test revealed no statistically significant differences in APT side to side in any of the conditions ($p=.472-.619$). Independent samples t-test revealed no statistically significant differences in APT between transtibial and transfemoral amputees. Statistical analysis of PEQ and ODI answers also revealed no statistically significant differences between level of amputation.

Discussion: The lack of statistically significant differences in APT did not agree with a previous preliminary study, which did find a statistically significant difference in APT between the sound side and amputee side. Due to a lack of statistical significance, limited sample size, and conflicting results with a previous study, further research is warranted regarding APT prevalence in the amputee population. It would also be beneficial for further research on APT prevalence in a normal population to allow for future age and gender comparisons.

Abstract No. 35 (Student_Graduate)

Title

Structural Modification of (-)-N6-(2-(4-(Biphenyl-4-yl)piperazin-1-yl)-ethyl)-N6-

propyl-4,5,6,7-tetrahydrobenzo[d]thiazole-2,6-diamine (D-264): An Effort To improve the blood brain barrier crossing ability and multifunctional property in lead compounds for the treatment of Parkinson's Disease.

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Authors

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Reith, 1 Alope Dutta.

Abstract

Parkinson's disease (PD) is an age-related, progressive neurodegeneration disorder, characterized by gradual loss of dopaminergic neurons in the substantia nigra region of the brain. The currently available therapies provide only symptomatic relief without addressing the underlying pathophysiology. Our hypothesis is to develop multifunctional ligands, with D2/D3 agonist, antioxidant and neuroprotection property. The titled compound is one of our lead molecule which has shown neuroprotection property in both in-vitro and in-vivo animal model of PD. The goal behind this study is to enhance the entry of the titled compound into the brain without compromising its agonist potency. The structural modification is mainly centered around the introduction of hydroxyl group at various positions on the accessory binding biphenyl ring of this hybrid molecule. This modification will reduce the lipophilicity and the introduction of more than one hydroxyl group at a suitable position can further potentiate its antioxidant and neuroprotection property. Various analogs of the titled compound have been designed and synthesized. Compound D-433 with hydroxyl substitution exhibited the highest selectivity in binding (D2/D3=341) and functional GTP γ ... S assay (D2/D3 =248).

Interestingly, in both reserpine-induced hypolocomotion and 6-OHDA lesioned animal model of PD, D-433 exhibited long duration of action over the D-264. This is a clear indication of more facile entry of D-433 into the brain. While their antioxidant, neuroprotection and alpha synuclein aggregation inhibition assays are currently under study.

Abstract No. 36 (Student_Graduate)

Title

Reliability of CROM Postural Measurements in Asymptomatic Females over 40

Affiliations

Wayne State University Eugene Applebaum
College of Pharmacy and Health Science

Authors

Katherine Vezina SPT, Julie Khuong SPT,
Nicole Widak SPT, Diane Adamo PhD, OTR,
Kim Dunleavy PhD, PT, OCS,

Abstract

INTRODUCTION/CLINICAL SIGNIFICANCE: The cervical range of motion (CROM) instrument has been shown to have good reliability and validity for range of motion (ROM) measurements, and for measurement of forward head position from C7 (FHP). The use of the portable CROM for cervicothoracic postural position measurement might be useful rather than requiring sophisticated instrumentation or photogrammetry. The purpose of this study was to establish the intra-rater, inter-rater reliability, measurement error and minimal detectable change at the 95% CI (MDC95) of the CROM device for: 1) sagittal plane distances of the occiput (OP), C7, and maximum thoracic width (TW) from the bridge of the CROM 2) the upper cervical angle (UCA), and 3) distances of the postural points to a central plumb line (PL). METHODS: A

within-subjects repeated measures descriptive design was conducted using 13 female participants over the age of 40 without neck pain. Subjects were excluded if there was a history of cervical pain, whiplash, hypermobility or any other medical conditions. CROM postural measurements were conducted simultaneously by two researchers in three seated postural conditions: 1) habitual (HAB - no instructions), 2) perceived optimal (PO - sit in your best posture) and 3) therapist-corrected (TC - verbal, visual and tactile cues to obtain an optimal posture with respect to a central plumb line). A laser plumb line was positioned at the greater trochanter to reflect the PL. Distances were recorded from the nose to the OP, C7, TW as well as the PL on the CROM horizontal arm. Relative distances to PL were calculated. Intra-class correlation coefficients were calculated to determine intra-rater reliability (ICC3,1) and inter-rater reliability (ICC2,k) and repeated measure ANOVAs used to establish differences across postural conditions. RESULTS: Intra-rater reliability for both examiners was good (ICC3,1 = 0.76 – 0.93) and inter-rater reliability was very good (ICC2,k = 0.90-1.00) for variables in all conditions. The calculated distances of the postural points to PL showed lower intra-rater reliability (ICC3,1 0.19-0.89), while inter-rater reliability was very good (ICC2,k 0.97-1.00). The postural distances were significantly smaller in PO posture than TC position ($p < 0.01$), along with TW being smaller than the habitual position ($p < 0.01$). UCA was significantly more flexed in TC posture compared to HAB & PO postures ($p < 0.001$). CONCLUSIONS: Good intra-rater reliability, excellent inter-rater reliability coefficients and the ability to reflect changes in postural position support the use of the CROM as a reliable clinical tool for recording cervicothoracic postural measurements for OP, C7, TW & UCA. Calculated values from OP and C7 to PL are sufficiently reliable while TW-PL requires use of means. SEM% was low for all variables with moderate error for PL and low to moderate relative to PL. MDC95% was low to moderate for all variables except for PL and calculated distances to PL. Limitations of the measurements include small increments and

possibility of angular displacement of the CROM

Abstract No. 37 (Student_Graduate)

Title

Internet Analysis of Delayed and Alternative Child Immunization Schedules

Affiliations

Wayne State University, Eugene Applebaum College of Pharmacy and Health Science

Authors

Erin L. Beattie, PharmD Candidate ... Emily T. Martin, M.P.H., Ph.D.

Abstract

Background

An increasing number of parents are choosing to delay vaccines or use alternative immunization schedules for their children. The internet is one of the sources that parents use in deciding how they vaccinate their children ... however, little research has been conducted to characterize available information. There are internet sources that support the Centers for Disease Control recommended child immunization schedule as well as a number of sources that promote the use of alternative schedules.

Objective

This internet analysis was designed to find suggested child immunization schedules and compare them to the CDC recommended schedule. The time it takes to complete each schedule, the vaccine preventable diseases covered and the reasons for deviation from the CDC schedule were evaluated.

Methods

An internet search was done on Sept. 12, 2012 using the following search terms entered into the Google search engine: "Alternative

immunization schedule”, “alternative vaccine schedule”, “delayed immunization schedule”, and “delayed vaccine schedule”. The first two pages of results for each search term were examined for information about suggested alternative schedules and whether the content was “pro-alternative”, “anti-alternative”, or neutral unless any of the following exclusion criteria were met: Inactive link, video result, non-English site, not relevant to pediatric vaccine administration, news result, medical journal site, newsgroup page, or listserv page. The alternative immunization schedules referred to in these search results were compared to the CDC recommendations.

Results

A total of nine suggested schedules were identified from twenty five unique results that met the inclusion criteria. Eleven results were classified as anti-alternative immunization sites, eleven as pro-alternative and three as neutral. The schedules varied greatly in the recommendations and ranged from full but delayed coverage of CDC recommended immunizations to natural immunity only. The reasons discussed for the suggested deviations from the CDC schedule include safety concerns (toxic additives, links to autism and immune disorders, excessively early administration, general adverse reactions), excessive immunizations during a single visit, absence of disease exposure, superiority of natural immunity, and distrust of the CDC.

Conclusions

The delayed and alternative schedules found during this analysis do not fulfill kindergarten immunization requirements and more visits to the doctor are required to follow the schedules. More research is needed to analyze the information caregivers encounter when searching the internet about child immunization recommendations.

Abstract No. 38 (Faculty)

Title

Synthesis and Characterization of Istatin Inhibitors of N5-CAIR Synthetase

Affiliations

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Firestine

Abstract

Antibiotics are arguable one of the most important discoveries in modern medicine. Unfortunately, their dominance over bacterial infections is slowly being eroded by the rise of organisms resistant to antimicrobial drugs. Thus, there is clearly a need for the continued development of novel antibiotics that target previously under-explored pathways. One such pathway is de novo purine biosynthesis. Previous research has shown that the pathway is fundamentally different between microorganisms and humans. The divergence is centered on the microbial enzymes, N5-carboxyaminoimidazole ribonucleotide (N5-CAIR) synthetase. Humans do not require this enzyme nor do they possess a homolog of the protein. Previous research in our laboratory has discovered that isatin and its analogs inhibit N5-CAIR synthetase. To investigate these inhibitors, we synthesized and examined isatin analogs for their ability to inhibit N5-CAIR synthetase. From these studies, we determined the following SAR principles: i. small substituents off of N1 are preferred ... ii. the amide carbonyl group at C2 is required ... iii. the 3 position requires a double bond to an atom which contains at least one lone-pair of electrons ... iv. electron-withdrawing groups are preferred on the aromatic ring ... v. preferred substitution on the

aromatic ring is 5≈ ... 7>6>>4 ... 5,7-disubstitution is tolerated. The antibacterial properties of these compounds against *Staphylococcus aureus* were examined. We found that several compounds inhibited bacterial ... however, growth inhibition could not be recovered by the addition of purines indicating that the antibacterial effects of these agents was not due to inhibition of the purine pathway.

Abstract No. 39 ()

Title

Safety and Efficacy of a Strategy to Prevent Drug-Induced Nephrotoxicity in High-Risk Patients (STOP-NT)

Affiliations

Wayne State University Eugene Applebaum College of Pharmacy ... Henry Ford Hospital ...

Authors

Joseph J Carreno, PharmD ... Susan L Davis, PharmD ... Chambers M Chambers, PharmD ... Jose A Vazquez, MD

Abstract

Background: Numerous risk factors linking vancomycin (VAN) to nephrotoxicity (NT) have been identified. In several clinical trials, alternative therapeutic agents (ATA) have been associated with a lower incidence of NT. However, it is not known if the use of ATA impacts NT in high-risk populations. The objective of this study was to determine if substituting VAN for ATA reduces NT in high-risk populations.

Methods: This is an ongoing prospective, single-blinded, single-center, randomized, controlled trial. Inclusion criteria: age ≥ ... 18 yrs, receiving dose-optimized VAN for empiric or definitive treatment of healthcare associated pneumonia (HCAP), osteomyelitis/septic arthritis (OST),

endocarditis/bacteremia (BAC), or acute bacterial skin and skin structure infections (ABSSSI), expected to receive VAN or ATA ≥ ... 72 hrs, and had ≥ ... 2 risk factors for NT. Exclusion criteria: active acute kidney injury, end-stage renal disease, receipt of > 4 g of VAN, receipt of > 72 hrs of therapy prior to enrollment, pregnancy or absolute neutrophil count < 1000/mm³. Patients were randomized to VAN or to ATA stratified by disease state (ceftaroline [ABSSSI], daptomycin [ABSSSI, BAC, OST] or linezolid [HCAP, ABSSSI, OST]). Primary outcome: VAN Consensus Statement defined NT (Am J Health Syst Pharm, 2009). Secondary outcomes: Acute Kidney Injury Network Modified Definition of NT (AKIN-NT) (Crit Care, 2007) and Clinical Success. Outcomes are determined by investigators blinded to the treatment group.

Results: 64 pts have been randomized: stratified into HCAP (23), OST (8), BAC (10), and ABSSSI (25). Baseline characteristics were similar between both groups with respect to age, sex, NT risk factors, initial ICU admission and medical service. In the evaluable population (n = 64), when comparing VAN vs. ATA, the incidence of NT was 9.4% vs. 9.4% (p = 1.0), while AKIN-NT was 34.4% vs. 31.2% (p = 0.79), respectively.

Conclusions: In this preliminary analysis, comparing VAN vs stratified ATA, there appears to be no difference in the incidence of NT or AKIN-NT in either study group. A larger sample size is needed to fully elucidate any potential differences between these groups and the impact on healthcare costs.

Abstract No. 40 (Student_Graduate)

Title

The Effects of Liraglutide on Tacrolimus Pharmacokinetics, Renal Function, and Adverse Events in Kidney Transplant Recipients: Preliminary Data

Affiliations

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Authors

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Genni Lipari, PharmD Candidate III1 ... Anita Patel, MD1,2 ... Steve Gray, RN, BSN2 ...
Andrea Dwyer, RD2 ... Francine D. Salinitri, PharmD1,3 ... Nicole R. Pinelli, PharmD, MS, CDE1,2

Abstract

Purpose: The primary objective of this study was to investigate the effect of liraglutide on tacrolimus pharmacokinetics (AUC0-12h and trough levels) in kidney transplant recipients. The secondary objectives included assessment of kidney function and adverse events in this population.

Methods: Non-pregnant, clinically stable adult (\geq ... 18 years) kidney transplant recipients receiving unchanged doses of tacrolimus for \geq ... 4 weeks (goal trough concentration 5-15 ng/mL) were included in this study. Patients with documented diabetes mellitus and/or varying doses of steroids were excluded. Experiments conducted were prospective, non-randomized, open-label and used a two-period pre- and post-design. Pharmacokinetic profiling was performed before and after self-administration of a 21-day course of liraglutide (0.6 mg for 1 week, followed by 1.2 mg during week 2, and 1.8 mg during week 3). The primary outcome was change in tacrolimus AUC0-12h as measured with a previously validated multiple regression derived limited sampling strategy using blood samples obtained before the morning dose of tacrolimus and at 1, 2, and 4 hours post-dose. Safety and tolerability were captured by means of laboratory assessment,

adverse event recording and investigator observation. Data are expressed as means \pm SD or percentages unless otherwise noted. Descriptive statistics were performed for this preliminary safety assessment.

Results: Five patients have been enrolled to date (55.4 \pm 8.2 years, 60% male, 80% African American, BMI 30.1 \pm 6.2 kg/m², eGFR 93.0 \pm 21.3 mL/min/1.73m², 40% prediabetes, 80% on chronic steroid therapy). Compared to baseline, non-dose normalized tacrolimus AUC0-12h appeared reduced following co-administration with liraglutide ... however, trough concentrations remained within the therapeutic goal. No patients experienced >0.5 mg/dL increase in serum creatinine from baseline. No hypoglycemia or serious adverse events related to liraglutide therapy were reported. Nausea, reduced appetite, headache, injection site pain, and weakness were reported by 50% (n=2). Indigestion was experienced by 25% (n=1).

Conclusion: These preliminary data suggest co-administration of liraglutide with tacrolimus may reduce non-dose normalized tacrolimus AUC0-12h in kidney transplant recipients ... however, clinically significant alterations in trough tacrolimus concentrations were not observed. Liraglutide administration appears relatively safe in kidney transplant recipients and adverse events are similar to those reported in the non-kidney transplant population.

Sponsored by the EACPHS FRAP Young Investigator Award to Nicole R. Pinelli.
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Abstract No. 41 (Post_Doctoral_Fellow)

Title

An Evaluation of Ceftaroline (CPT) and Daptomycin (DAP) or Vancomycin (VAN) Combination Against an Isogenic Methicillin-Resistant Staphylococcus aureus (MRSA)/ Vancomycin Intermediate S. aureus (VISA) Pair

in an In Vitro
Pharmacokinetic/Pharmacodynamic (PK/PD)
Model.

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Abstract

Background: Infections caused by MRSA with reduced susceptibility to VAN and DAP are difficult to treat with currently available antimicrobials and may be associated with poor outcomes. New agents and novel combinations must be explored in order to establish safer and more effective alternatives for managing infections caused by MRSA with reduced susceptibility to DAP and VAN. The purpose of this study was to evaluate the novel combination of CPT + DAP and CPT + VAN in an in vitro PK/PD model.

Methods: The activity of simulations of CPT-fosamil 600mg q8h (fCmax 15.2mg/L, t1/2 2.3h), DAP 10mg/kg/day (fCmax 11.3mg/L, t1/2 8h) VAN 2g q12h (fCmax 30mg/L, t1/2 6h), CPT + DAP and CPT + VAN were evaluated against a clinical, isogenic DAP susceptible (DS) hVISA/DAP non-susceptible (DNS) VISA strain pair, in a one compartment in vitro PK/PD model over 96h. Therapeutic enhancement of combinations was defined as $\geq 2 \log_{10}$ reduction in CFU/ml over the most active agent alone. Human cathelicidin LL37 (128 μ M) killing was examined at 1.5 and 3 h against both strains grown in the presence or absence of CPT 0.1 mg/L. DAP depolarization with and without CPT was evaluated. Cell wall thickness (CWT) was measured by transmission electron microscopy.

Results:

D712 D592
log₁₀CFU/ml at 96h MIC log₁₀CFU/ml 96h
MIC
DAP 8.29 \pm 0.03* 4 5.92 \pm 0.18* 0.5
VAN 6.82 \pm 0.04* 4 6.08 \pm 0.33* 2
CPT 4.63 \pm 0.19* 0.5 6.87 \pm 1.15* 1
DAP+CPT 1.15 \pm 0.21# — 1 \pm 0.00# —
VAN+CPT 3.18 \pm 0.49* — 1.75 \pm 0.21# —

- Significantly different than D+C (p \leq ... 0.001)

Therapeutic enhancement

CPT exposure reduced mean CWT by 8.94nm (P<0.001), DAP+CPT exposure increased mean CWT by 2.42nm (P=0.02)

No resistant mutants were recovered in any of the models. CPT exposure enhanced DAP induced depolarization (81.7% vs 72.3% P=0.03) and killing by LL37 (p<0.01).
Conclusions: The combination of DAP + CPT appears to be a potent combination with rapid and sustained bactericidal activity against both DS as well as DNS strains. CPT was more active against the DNS VISA than the DS hVISA supporting the “seesaw” hypothesis.

Abstract No. 42 (Student_Graduate)

Title

Automated venous thromboembolism risk assessment and its effect on patient prophylaxis

Affiliations

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College of Pharmacy and Health Sciences,
Wayne State University

Authors

Geoffrey Morgan Pharm.D., Emily Fisher,
Kevin Costa, Cassandra Petros, Sheila Wilhelm
Pharm.D., BCPS

Abstract

Chronic obstructive pulmonary disease (COPD) is a known risk factor for the development of venous thromboembolism (VTE) in hospitalized patients. These patients must be identified and given proper prophylaxis to prevent the formation of clots, which can cause an increase in morbidity and mortality. The objective of this study is to determine the impact of the implementation of an automated VTE risk assessment tool on anticoagulant selection in COPD patients, as well as its effect on safety outcomes and readmission rates.

The study protocol has been approved by the institutional review board. This retrospective review assesses the impact of the October 2011 implementation of a computerized VTE risk assessment tool at the Detroit Medical Center (DMC). Included patients will be between ages 18-89 and have been admitted between December 2009 and August 2012 for a COPD exacerbation defined by a documented International Classification of Diseases, Ninth Revision (ICD-9) code of 496.0 (COPD) and shortness of breath indicated in the history of present illness or first inpatient progress note following admission. Information including basic patient demographics (e.g. age, gender, height, and weight), serum creatinine, comorbidities, anticoagulation contraindications, and VTE risk factors will be collected from the Electronic Medical Record (EMR) of 3 DMC hospitals. The primary objective will be the number of eligible patients receiving VTE prophylaxis and if that prophylaxis matched hospital protocol. Secondary objectives include the number and percentage of ordered patient prophylaxis doses not administered, number of thromboses, major and minor bleeding events, and 30 day readmission rates. A comparison will be made to determine if prophylactic dosing affects readmission rates. Patient VTE risk scores will be hand calculated to assess the accuracy of the automated system.

Abstract No. 43 (Post_Doctoral_Fellow)

Title

Outcomes Associated with Vancomycin Intermediate Staphylococcus aureus (VISA) Bloodstream Infections (BSI)

Affiliations

Anti-Infective Research Laboratory, Wayne State University
Detroit Medical Center

Authors

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Jason Pogue, Pharm.D.
Anthony Casapao, Pharm.D.
Michael Rybak, Pharm.D., M.P.H.

Abstract

Background

Staphylococcus aureus has been a problematic Gram-positive organism due to continually evolving virulence and drug resistance. In the past decade, isolates with reduced susceptibility to vancomycin, such as vancomycin-intermediate S. aureus (VISA) and vancomycin-resistant S. aureus (VRSA) have emerged. Patient outcomes have been well described in patients with MRSA BSI with higher vancomycin MICs that remain in the susceptible range. However, due to limited cases, patient outcomes secondary to VISA BSI, remain largely unknown. The objective was to compare the patient failure outcomes between MRSA BSI with a vancomycin MIC of $\leq \dots$ 1 mg/L, 2 mg/L and 4-8mg/L.

Methods

Adult patients at the Detroit Medical Center with a positive blood culture for VISA from 2005 to 2011 were included. VISA patients were matched in a 1:1:1 ratio based upon severity of illness, age, and source of infection to patients

with MRSA bacteremia with vancomycin MICs of $\leq \dots$ 1 mg/L and 2 mg/L. Patients with hVISA were excluded. Data collected included: demographics, length of stay, culture and susceptibilities, drug therapy and patient outcomes.

Results

54 patients were included. There were no significant differences in patient demographics other than previous antimicrobial exposure and previous staphylococcal infection were more common among the VISA patients. Overall, patients with VISA bacteremia had worse outcomes than those with vancomycin MICs of $\leq \dots$ 1 mg/L and 2 mg/L with increased failure rates (67% vs. 28% vs. 11% ... $p = 0.002$) and a trend toward a longer length of stay, and increased mortality. Serum vancomycin concentrations were similar between the groups.

Conclusion

Patients with VISA BSI had significantly higher failure rates when compared to those with non-VISA strains.

poses a therapeutic challenge due to a paucity of pediatric data. Diagnoses of pediatric fibromyalgia, chronic regional pain syndrome and juvenile rheumatoid arthritis are increasing. These complex patients may have failed first line analgesic treatment when they present for multidisciplinary management. The serotonin norepinephrine reuptake inhibitor (SNRI) duloxetine approved for neuropathic pain including fibromyalgia (FM) for adults has limited data for pediatric use.

Objective: Report experience using duloxetine for adolescents with chronic neuropathic pain.

Methods: Case report series of adolescents managed by CHM pediatric multidisciplinary pain management clinic team (Pediatric Anesthesiologist, resident/fellow, physician assistant, clinical psychologist, clinical pharmacist, pharmacy students). Data abstracted from clinic chart and electronic medical record included demographic and clinical characteristics, medication history, self-report pain (Numerical Pain Rating NRS) and adverse effects.

Results: Five patients (13-17 years ... 4 female) received duloxetine 30-60 mg daily for pain diagnoses: FM, chronic regional pain syndrome (CRPS), leg pain and headache. Three had comorbid depression. Duration of pain condition was 0.5-5 years with pain scores $>5/10$ prior to duloxetine. Decision to prescribe duloxetine based on pain diagnosis, patient self-report, pain symptoms, comorbid conditions, analgesic history. Response evaluated during routine telephone calls (5 days after a prescription/dosage change) and during regular clinic appointments (every 6 weeks to 3 months). Percent reduction in pain score during duloxetine therapy was 0% to 38% (one patient reported complete resolution of pain). Length of duloxetine therapy was 1 month-5 years. Three patients reporting adverse reactions (all discontinued duloxetine: nausea, rash, and mild transient chest pain).

Conclusion: Our experience with duloxetine for pain management in an adolescent population has been limited by side effects and lack of

Abstract No. 44 (Student_Graduate)

Title

Experience with Duloxetine for Management of Chronic Neuropathic Pain in Adolescents

Affiliations

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Department of Anesthesia Children's Hospital of Michigan

Authors

Melanie Smallwood, PharmD Candidate 2014 ...
Suresh Thomas, MD ... Victoria Tutag-Lehr,
B.S. Pharm, PharmD

Abstract

Background: Management of chronic neuropathic pain for children and adolescents

efficacy. For neuropathic pain the accepted reduction is $\geq \dots 30\%$. Three patients in our series had this magnitude of response (33% ... 38% ... 100% reduction). Adolescents may experience more GI side effects (nausea, vomiting) with SNRIs compared with adults and therefore a consideration with duloxetine therapy. Adherence with duloxetine therapy which can be $\leq \dots 40\%$ for adolescents with chronic conditions was not verified. Adolescents with chronic neuropathic pain often have failed several analgesics and are seeking relief. Drug therapy represents one component of treatment and “first-line” tricyclic antidepressants (TCAs), gabapentanoids (gabapentin, pregabalin) may be limited by side effects, slow onset or poor response. Consideration of duloxetine as alternative analgesic after failure or intolerable side effects with gabapentanoids, TCAs or NSAIDs may be appropriate. We recommend use as part of a multidisciplinary approach with careful monitoring of adherence, response and adverse effects. Tricyclic antidepressants, serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, and (gabapentanoids) anticonvulsants remain agents of choice in these conditions due to their ability to target a wide range of mechanisms of action.

Abstract No. 45 (Post_Doctoral_Fellow)

Title

Targeted siRNA delivery using transferrin-polyethylenimine conjugate

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3 Department of Neurosurgery, Wayne State University, Detroit, MI

4 Barbara Ann Karmanos Cancer Institute, Detroit, MI

Authors

Na Hyung Kim¹, Venkatarreddy Nadithe¹, Danielle Batton¹, Archana Thakur^{2,4}, Lawrence Lum^{2,4}, Nicholas Szerlip^{3,4}, Olivia M Merkel^{1,4}

Abstract

RNA interference (RNAi) is a promising therapeutic tool for downregulating clinically relevant genes¹. Despite its great therapeutic potential and recent progress in research about RNAi therapy, efficient delivery of small interference RNA (siRNA) to target cells with minimal toxicity is still one of the major challenges^{1,2}. In order to meet the challenge, we designed a targeted siRNA delivery system consisting of transferrin (Tf) and low molecular weight polyethyleneimine (PEI), which can specifically deliver siRNA to transferrin receptor (TfR)-overexpressing cells with high transfection efficiency but reduced cytotoxicity compared to high molecular weight PEI³⁻⁵. Here, using the Tf-PEI conjugate, we demonstrated the targeted delivery of siRNA to activated primary T cells, which play a central role in inflammatory diseases including asthma, and to patient derived glioblastoma multiforme (GBM) cells, the most common and lethal primary malignant brain tumor^{6,7}.

Transferrin was conjugated with 5kDa PEI using dimethylsuberimidate as a crosslinking agent, and resulting Tf-PEI conjugate was purified by ion exchange column chromatography and membrane ultrafiltration⁸. According to the SYBR Gold assay, the Tf-PEI conjugate condensed siRNA as efficiently as unconjugated PEI, showing complete condensation at N/P 5 which was chosen for the following experiments. After the overexpression of transferrin receptor in activated T cells and GBM cells was confirmed using CD71 antibody, the uptake of Tf-PEI/siRNA complexes was examined using flow cytometry and confocal microscopy. In activated T cells, the uptake of

fluorescently-labeled siRNA mediated by Tf-PEI (mean fluorescence intensity, MFI: 116) was more efficient than the siRNA uptake with positive control, Lipofectamine (MFI:30) as well as with unconjugated PEI (MFI:10). No siRNA taken up into the T cells with very low TfR expression confirmed the specificity of Tf-PEI for TfR overexpressing activated T cells. In GBM cells, with Tf-PEI conjugate, 99% of live cells showed an uptake of siRNA (MFI:146), while siRNA was taken up by 15% of live cells with unconjugated PEI (MFI:10). Furthermore, Tf-PEI/siRNA complexes achieved 60% knockdown of GAPDH gene expression, which was comparable with Lipofectamine. Unconjugated PEI/siRNA complexes did not show any gene silencing effect.

Based on the enhanced and specific uptake and gene silencing results, we expect our Tf-PEI conjugate to be a promising siRNA delivery system for future in vitro and in vivo studies with therapeutic target genes against asthma or GBM.

References

1. Kole R. et al., *Nat. Rev. Drug Discov.*, 2012, 11(2):125-140.
2. Oh Y.K. and Park T.G., *Adv. Drug Deliv. Rev.*, 2009, 61(10):850-862.
3. Daniels T.R. et al., *Biochim. Biophys. Acta*, 2012, 1820(3):291-317.
4. Neckers L.M. and Cossman J., *Proc. Natl. Acad. Sci.*, 1983, 80(11):3494-3498.
5. Kleemann E. et al., *J. Drug Target.*, 2009, 17(8):638-651.
6. Jeffery P.K., *Br. Med. Bull.*, 1992, 48(1):23-39.
7. Guo D. et al., *Expert Opin. Biol. Ther.*, 2010, 10(6):927-936.
8. Koppu S. et al., *J. Control. Release*, 2010, 143(2):215-221

Abstract No. 46 (Post_Doctoral_Fellow)

Title

DUAL-FUNCTION CXCR4 ANTAGONIST POLYPLEXES TO DELIVER GENE THERAPY AND INHIBIT CANCER CELL INVASION

Affiliations

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Authors

Jing Li, PhD ... Yu Zhu, BS ... David Oupicky, PhD

Abstract

Bioreducible polycations have been investigated widely as synthetic gene delivery vectors for cancer therapy. Traditionally, polycations have been viewed as pharmacologically inert components of delivery systems. Herein we describe a novel class of polycations that not only deliver plasmid DNA but also function as CXCR4 antagonists that inhibit cancer cell invasion and thus could limit metastasis in various approaches to gene therapy for cancer. CXCR4 is a chemokine receptor overexpressed in various cancer cells. In response to binding its ligand CXCL12, CXCR4 triggers the migration and invasion of cancer cells, which has been shown to promote tumor metastasis. AMD3100 (Plerixafor) as a FDA approved CXCR4 antagonist, is known to block the CXCR4-CXCL12 interactions and inhibit tumor invasion. Here we synthesized a reducible Poly-AMD3100 (RPA) by direct Michael addition polymerization of AMD3100 with a disulfide-containing bisacrylamide. The RPA polymer showed remarkably low cytotoxicity and exhibited high in vitro transfection efficiency comparable with 25 kDa PEI in various cell lines. The CXCR4 antagonism was evaluated by a receptor redistribution assay that monitors the internalization of GFP-tagged CXCR4 receptor

into endosomes upon CXCL12 stimulation. Both RPA and RPA/DNA polyplexes showed inhibition of receptor internalization compared with positive control AMD3100. The antimetastatic efficiency of RPA and RPA/DNA polyplexes was further confirmed by blocking invasion of 71-77% of CXCR4+ U2OS cells in cell invasion assay. In conclusion, we have developed a synthetic polycation that functions as a CXCR4 antagonist capable of blocking cancer cell invasion while simultaneously delivering plasmid DNA and mediating transfection.

Abstract No. 47 (Post_Doctoral_Fellow)

Title

Cationic Nylon-3 based poly-beta-peptides for siRNA delivery

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Authors

Venkatareddy Nadithe (1), Runhui Liu (2,3), Na Hyung Kim (1), Kristyn S. Masters (3), Samuel H Gellman (2), Olivia M Merkel(1,4)

Abstract

The clinical translation of RNA interference (RNAi) requires biocompatible siRNA delivery systems[1]. Poly-beta-peptides (nylon-3 materials) with biocompatible backbone have attracted strong interest in their biological applications. They are synthesized by ring-opening polymerization (ROP) of beta-lactams

bearing a cationic and hydrophobic side chain. Diverse functional groups can also be placed at the nylon-3 chain termini, which enables the tuning of physical properties[2].

Panels of nylon-3 polymers are synthesized and classified into three groups depending on the content of the two subunits: 1) 60% cationic and 40% hydrophobic, 2) 40% cationic and 60% hydrophobic and 3) 90% cationic and 10% hydrophobic. Molecular weights of the polymers within each group are varied between 6 kDa and 45 kDa. Polymers within group 1, 2 and 3 efficiently condensed siRNA at very low N/P ratios of 2, 5 and 2 respectively. Preliminary results identified several potential candidates with promising transfection capability (cell uptake), luciferase knockdown, and low cytotoxicity in H1299/Luc cells at N/P ratios below 5. The ability of the nylon-3 polymers to form stable polyplexes and protect siRNA from degradation proves the usefulness in RNAi interference.

- 1.Li, C.X., et al., Cell Cycle, 2006. 5(18): p. 2103-9.
- 2.Zhang, J., et al., J Am Chem Soc, 2009. 131(4): p. 1589-97.

Abstract No. 48 (Faculty)

Title

Ceramide Synthase 6 Knockdown Suppresses Apoptosis after Photodynamic Therapy in Human Head and Neck Squamous Carcinoma Cells

Affiliations

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Authors

Duska Separovic, Paul Breen, Nicholas Joseph, Jacek Bielawski, Jason S. Pierce, Eric Van Buren and Tatyana I. Gudz

Abstract

Background: The effectiveness of photodynamic therapy (PDT) for cancer treatment correlates with apoptosis. We observed that suppression of de novo-generated sphingolipids, e.g. ceramide, renders cells resistant to apoptosis post-PDT. Ceramide synthase 6 (CerS6) has been implicated in apoptosis after various stimuli. **Aim:** To investigate the involvement of down-regulation of CerS6 in apoptosis and its impact on the sphingolipid profile post-PDT with the silicon phthalocyanine Pc 4 in a human head and neck squamous carcinoma cell line. **Materials and Methods:** Besides siRNA transfections and PDT treatment, immunoblotting for protein expression, mass spectrometry for sphingolipid analysis, spectrofluometry and flow cytometry for apoptotic marker detection, and trypan blue assay for cytotoxicity assessment, were used. **Results:** CerS6 knockdown led to reduction in PDT-induced DEVDase activation, mitochondrial depolarization, apoptosis and cell death. CerS6 knockdown was associated with selective decreases in ceramides and dihydroceramides, markedly of C18-dihydroceramide, post-PDT. **Conclusion:** CerS6 might be a novel therapeutic target for regulating apoptotic resistance to PDT.

Abstract No. 49 (Student_Graduate)

Title

Adherence to treatment guidelines for the inpatient management of COPD exacerbations and impact on patient outcomes

Affiliations

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Authors

Emily Fisher ... Geoffrey Morgan, Pharm.D. ... Kevin Costa ... Cassandra Petros ... Sheila Wilhelm, Pharm.D., BCPS

Abstract

In patients with chronic obstructive pulmonary disease (COPD), exacerbations lead to increased morbidity and hospitalizations. It is important to optimally treat these exacerbations to prevent future morbidity as well as to decrease the number of hospital readmissions. The GOLD guidelines describe an approach to managing patients with COPD exacerbations, and this study will look at how closely the treatment of patients admitted to Harper University Hospital, Hutzel Women's Hospital, and Rehabilitation Institute of Michigan follows these recommendations. The impact of appropriate treatment on patient outcomes will be assessed by examining length of stay and 30-day readmission rate data.

This retrospective chart review has been approved by the Institutional Review Board. Potential study subjects admitted to Harper University Hospital, Hutzel Women's Hospital, or the Rehabilitation Institute of Michigan from December 2010 to September 2011 and November 2011 to August 2012 will be identified by ICD 9 code (496 Chronic airway obstruction, not elsewhere classified). Approximately 400 of these patients will be randomly selected and assessed for inclusion. Eligible patients must be between the ages of 18-89 and have shortness of breath documented in the history and physical or first progress note for the selected admission date. Data collected will include patient demographics, pulmonary medications administered, number of inhalers dispensed from pharmacy per patient order, season of admission, length of stay, readmission

and cause (if applicable), comorbidity score (based on Charlson Comorbidity Index), and whether a standardized COPD order set was used. The primary outcome is to determine how well treatment of COPD exacerbations followed the GOLD guidelines, which will be assessed by recording the medication classes used and comparing that to guideline recommendations. Secondary outcomes include calculating average admission rates per season, and whether appropriate treatment according to the guidelines impacts length of stay and 30-day readmission rates.

Abstract No. 50 (Faculty)

Title

Pain Assessment in Hospitalized Children and Adolescents: What is the Score? Preliminary Analysis

Affiliations

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Authors

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Abstract

Background: Appropriate pain assessment and management is essential for children because they perceive and react to pain with exaggerated physiologic responses compared to adults. Suboptimal pain management during infancy and childhood may have detrimental effects on behavior and development. Developmentally appropriate pain assessments used to document pain at baseline and re-assess after treatment or analgesic administration can evaluate

effectiveness of interventions. We describe pain management for children using EMR documentation of pain scores and analgesic administration. Objectives: To evaluate: 1) pain assessment for children receiving analgesics at Children's Hospital of Michigan, measured by percent change in pain score documented at admission, at discharge and prior to and after administration of an opioid analgesic ... 2) characteristics of patients with persistent moderate-severe pain (\geq ... 5/10). Methods: Retrospective review of electronic medical records of inpatient or surgical outpatients aged 3 months to \leq ... 18 years treated with analgesics for acute or chronic pain during period January 2011-October 2011. Data abstracted included demographic and clinical characteristics, pain diagnosis, analgesic type, dose, and frequency, pain assessment score, pain score pre and post analgesic, pain score at admission and discharge, opioid related adverse effects, nondrug interventions and discharge prescriptions . Results: The patient cohort comprised 100 children, of whom 59% were male, 62% were nonwhite, with an average age of 6.3 years and average weight of 27.8 kg. Over half (58%) were inpatient admissions with 43% having a previous admission. Home opioid use reported by 10%. Common admitting medical services included: general surgical (28%) ... infectious disease (13%) ... orthopaedic surgery (12%) ... pulmonary (11%) ... and neurosurgery (8%). The vast majority of patients (96%) were treated for acute pain. Average pain score at admission was 2.0 (\pm 3.3 ... 0-10), while the pain score at discharge was 1.3 (\pm 2 ... 0-10) corresponding to mean reduction of 34% (\pm 45% ... 0-100). Various analgesics were used and included: morphine (88%) ... fentanyl (61%) ... codeine (41%) ... hydrocodone (8%) ... meperidine (4%) ... hydromorphone (2%) ... NSAIDs (ibuprofen 15% ... ketorolac 4%) ... acetaminophen (64%). Mean length of opioid administration was 58 h. Pain score pre and post-intervention documentation data was available for 55% of patients with 78% overall mean reduction in pain score. Common analgesic adverse effects were nausea and vomiting (43%). Opioid analgesics prescribed at discharge for 40%. Higher pain score at admission was associated with previous hospital admission, prior opioid

use, and longer duration of opioid treatment ($p>0.05$). Increased pain score on discharge compared to admission was reported (26%) in patients with complex surgical conditions. Conclusion: Majority of pediatric patients studied received morphine for primarily acute painful procedures. Not all children experienced complete relief during treatment, yet when documented, patients had a 78% reduction in pain. However, the challenge remains to treat patients with persistent pain $\geq \dots 5/10$, especially at time of discharge. We hope to improve management of children with pain scores $\geq \dots 5$ and develop criteria for appropriate early referral to pediatric interdisciplinary pain management programs.

Abstract No. 51 (Student_Graduate)

Title

FOOT CARE AND EXERCISE BEHAVIORS/
KNOWLEDGE AT A DIABETES
EDUCATION & WELLNESS STUDENT-RUN
CLINIC – A PILOT STUDY.

Affiliations

Wayne State University, Detroit, MI.

Authors

Cierra Boprie SPT, Ashleigh Brueck SPT,
Alexandra Patterson-Tichy SPT, Martha Schiller
DPT ...

Abstract

INTRODUCTION: Management of type II diabetes includes pharmaceutical and medical care, exercise, regular foot exams and incorporating healthy lifestyles. Previous research reports deficits in education and knowledge regarding the importance of exercise and foot care. A multidisciplinary Diabetes Education and Wellness (DEW) clinic has been developed in collaboration with Wayne State University and the SAY Detroit Family Health

Care Clinic to provide education to underserved women with type II diabetes. The purpose of this study is to determine the short term effects of a standardized educational program regarding exercise and foot care on knowledge and behavior changes in an urban under/insured diabetic population. METHODS: This was a prospective, descriptive pilot study with a pre/post design. Eleven participants with type II diabetes were recruited from the DEW Clinic. Participants were scheduled to attend the DEW clinic for a total of 4 visits. All participants received diabetes foot care, exercise education and a home program provided by physical therapy student volunteers and all completed The Summary of Diabetes Self-care Activities Measure (SDCA) and The Spoken Knowledge in Low Literacy in Diabetes Scale (SKILLD) at visit one and four. Outcomes were analyzed pre and post intervention. Descriptive statistics were analyzed using SPSS. RESULTS: Data was analyzed for 11 subjects, all African American women with a mean age of 50.5 (SD 4.5). Subjects reported that foot examinations and exercise were important for controlling /preventing complications from diabetes, with a mean of 4.60 (SD1.23) and 4.80 (SD .42) respectively on a scale of 0 to 5. At visit 1, subjects reported participating in foot care activities (foot and shoe inspection) on average 2.95 days/week. Of those that completed all 4 visits, the average increased to 7 days/week. At visit 1, subjects reported participating in physical activity or exercise on average for 3.05 days/week. Of those that completed all 4 visits, the average increased to 6.5 days/week. Score on the SKILLD 10 knowledge questions pre-intervention was a mean of 4.91(2.77). Of those that completed all 4 visits, this increased to 8.0 (1.41). DISCUSSION: The majority of participants indicated that exercise and foot exams were important with controlling and preventing complications from diabetes but their frequency of behavior at visit one were not at the recommended levels. Preliminary data are encouraging with trends demonstrating an improvement in knowledge and short term behavior changes with respect to exercise and foot care. CONCLUSION: Change in knowledge and frequency in behaviors relating to foot care and exercise were made by subjects

participating at the DEW clinic. This is a positive step in diabetes management and a possible benefit of physical therapy intervention at the DEW clinic. ACKNOWLEDGMENTS: A special gratitude to the SAY Detroit Family Health Clinic, volunteers and donors for making this project possible.

Abstract No. 52 (Student_Graduate)

Title

The Effects of Liraglutide on Blood Glucose and Satiety Response in Kidney Transplant Recipients: Preliminary Data

Affiliations

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3. Oakwood Hospital and Medical Center, Department of Pharmacy Services, Dearborn, Michigan

Authors

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Andrea Dwyer, RD2 ...
Francine D. Salinitri, PharmD1,3 ...
Nicole R. Pinelli, PharmD, MS, CDE1,2

Abstract

Purpose: The objective of this study was to investigate the effect of liraglutide on blood glucose concentrations and satiety response in kidney transplant recipients.

Methods: Non-pregnant, clinically stable adult (\geq ... 18 years) kidney transplant recipients receiving unchanged doses of tacrolimus for ³⁴

weeks (goal trough concentration 5-15 ng/mL) were included in this study. Patients with documented diabetes mellitus and/or varying doses of steroids were excluded. Experiments conducted were prospective, non-randomized, open-label and used a two-period pre- and post-design. Experiments were performed before and after self-administration of a 21-day course of liraglutide (0.6 mg for 1 week, followed by 1.2 mg during week 2, and 1.8 mg during week 3). Blood glucose levels were measured at baseline (prior to tacrolimus administration) and at 60 and 120 minutes after completion of a standardized test meal. Caloric intake (kcal), food intake (grams), fluid ingestion (milliliters) and macronutrient content of meals were also measured. Body weight was collected. Data are expressed as means \pm SD or percentages unless otherwise noted. Descriptive statistics were performed for this preliminary analysis.

Results: Five patients have been enrolled to date (55.4 \pm 8.2 years, 60% male, 80% African American, BMI 30.1 \pm 6.2 kg/m², eGFR 93.0 \pm 21.3 mL/min/1.73m², 40% prediabetes, 80% on chronic steroid therapy). No differences were noted in blood glucose determinations at baseline (90.6 \pm 21.9 vs. 95.8 \pm 9.2). Liraglutide appeared to reduce blood glucose levels at 60 (131.4 \pm 21.5 vs. 106.8 \pm 9.2) and 120 minutes (127.2 \pm 13.6 vs. 108.8 \pm 7.9) following completion of the test meal. Compared to baseline, liraglutide did not reduce caloric intake, food intake, fluid ingestion, or macronutrient content of meals consumed. Liraglutide administration was associated with a reduction in body weight following 21 days of therapy (-2.1 \pm 1.3kg).

Conclusion: These preliminary data suggest liraglutide may reduce postprandial blood glucose concentrations in kidney transplant recipients. Liraglutide administration did not affect objective measures of satiety response in this study, but was associated with reduction in mean body weight.

Sponsored by the EACPHS FRAP Young Investigator Award to Nicole R. Pinelli.
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Abstract No. 53 ()

Title

Characteristics of Sensorimotor Function And Cursive Handwriting In Children With Fetal Alcohol Spectrum Disorder

Affiliations

Occupational Therapy Program, Wayne State University

Authors

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Abstract

INTRODUCTION. Children with Fetal Alcohol Spectrum Disorder (FASD) have complex and variable deficits in cognitive and social skills, as well as sensorimotor function. There is a paucity of research related to sensorimotor function^{1,2} and its occupational counterpart, handwriting, which is used in up to 60% of a typical school day³. There is no known study of both handwriting and related sensorimotor components in children with FASD. As handwriting assessment and intervention is a major role for occupational therapists in the school systems⁴, the purpose of this study was to examine sensorimotor and handwriting characteristics in children with FASD and to compare selected findings with a typically developing (TD) group matched by age and gender.

METHODS. Participants: 11 children with FASD (6 males ... age 9.6 ± 1.7 y) and a comparison group of 11 typically developing (TD) children matched by age and gender. Protocol: Clinical and handwriting tests were administered: two-point discrimination (sensation), tripod pinch force (strength) hand steadiness and grooved pegboard (coordination) ... Evaluation Test of Children's Handwriting (ETCH) (handwriting speed and legibility). In

addition, the Short Sensory Profile (SSP) and the Bruininks-Oseretsky Test of Motor Proficiency, Fine Motor Composite (FMC) were administered. Data Analysis: Descriptive data was developed for children with FASD, and independent t-tests were used for between-group comparisons. Significance was established at $p < 0.05$.

RESULTS. 10 of 11 children with FASD were below 2 standard deviations of normal sensory performance on the total SSP score, and all scores were below 2 standard deviations in the subcategory of auditory filtering. The FMC mean percentile was below average, as were the two subcategories of fine motor control and manual coordination. Of the sensorimotor tests, tactile sensation and pinch strength fell within normal limits. The scores of 9 of 11 children with FASD were below normal values for the grooved pegboard while supported hand steadiness was below normal values in 4 of 11 children. 4 of the 11 children could not produce cursive handwriting, compared to all 11 of TD children. When compared to age- and gender-matched children, sensorimotor skills differed only in hand steadiness ($t(20) = 2.21, p = .05$), while time to complete the ETCH approached significance ($t(16) = -2.1, p = .055$).

DISCUSSION. This is a preliminary study of handwriting and related sensorimotor components in children with FASD. These children showed typical strength and tactile sensation but impaired fine motor skills and coordination in comparison with TD children. These findings may partially explain some of the children's difficulty with cursive writing. Additionally, the presence of larger sensory processing issues may also impact handwriting performance. This pilot study provides direction for further research into relationships among sensorimotor issues and handwriting, and may help inform handwriting remediation for children with FASD.

1 Franklin et al, 2008

2 Simmons et al, 2012

3 McHale & Cermak, 1992

4 Vreeland, 1999

Abstract No. 54 (Faculty)

Title

Use of a unified learning style model to improve student self-directed learning in pharmacy students

Affiliations

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Authors

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Abstract

Purpose: Identify student learning preferences and use these preferences to enhance student life-long learning skills.

Methods: P1 pharmacy students completed a survey about exposure to learning style models and subsequently participated in a learning styles workshop early in the P2 year. The workshop included a 30-minute lecture defining learning style preferences and 2 hours to determine their preferences using: student self-reporting, learning preference survey, and faculty assessment. Students completed a “learning satisfaction survey” before the workshop and at the end of the semester to assess learning satisfaction, gain, motivation, time spent studying, and effort used when studying. Faculty and student agreement of learning styles were described using kappa values. Mean scores on the pre and post “learning satisfaction survey” were compared using paired t-test. In addition, the proportion of students answering “always” were compared pre versus post using McNemar’s test.

Results: Fourteen percent of P1 students were familiar with learning style preferences. 73 students completed the P2 workshop. Significant

agreement ($p \leq \dots 0.05$) was seen between faculty and student identification of visual, aural, reading, kinesthetic, active versus reflective, individual versus team, and competitive versus collaborative learning preference sub-categories. Significant agreement ($p \leq \dots 0.05$) was seen between faculty and survey identification of visual, aural, deductive versus inductive, individual versus team, and introvert versus extrovert. No significant changes were seen comparing mean scores on the learning satisfaction survey before and after the workshop. Increases were seen in the number of students answering “always” versus other categories in learning satisfaction (1 versus 5 students, $p=0.05$) and effort used when studying (0 versus 5 students, $p=0.03$).

Conclusions: The majority of students have limited exposure to learning style models. Student self-assessments and surveys could be used to determine learning styles. Educating students on their learning style preferences may improve their learning satisfaction and decrease their effort used when studying.

Abstract No. 55 (Student_Undergrad)

Title

The Impact of Physical and Mental Abuse on the Health of Black and White Women.

Affiliations

Occupational Therapy Program, Wayne State University

Authors

Angela Blanchard, Trudy Bazzzy

Abstract

Abstract
More than one in three women, (over 1.3 million women), in the United States has experienced violence and abuse at the hands of an intimate

partner in her lifetime. The consequences of intimate partner violence (IPV) are a societal and public health concern. IPV has a negative impact on women's mental and physical health, and research shows the economic cost of IPV to be around 5.8 billion dollars. The purpose of this study is to identify whether physical or mental violence has a more negative impact on women in society. We will also compare the negative impacts of IPV between black and white women. Our goal is to educate the community and identify whether certain populations can benefit from increased services.

This research is based on secondary data analysis from the 2000 National Violence Against Women Survey (NVAWS), and was collected in 1995. The sample included 8000 women 18 years and older from all 50 states who answered questions regarding their mental and physical health.

Results show black women experience IPV at a higher rate than white women. Black women are also more likely than whites to report alcohol use when they have experienced psychological and physical abuse. Likewise there is an increased association between poor perceived physical health among black women who have been psychologically or physically abused. We conclude that black women are in need of increased services to combat this problem.

Abstract No. 56 (Student_Graduate)

Title

Nephrology Transition of Care: Impact of a Student Pharmacist-Run Medication Reconciliation and Discharge Education Program on Patient Satisfaction in Hospitalized End Stage Renal Disease Patients

Affiliations

Oakwood Hospital and Medical Center

Authors

Alyssa Lopez, PharmD Candidate, Raymond Cha, PharmD, David A. Wilpula, PharmD, BCPS, Francine D. Salinitri, PharmD

Abstract

Background

Approximately 600,000 people in the United States live with end-stage renal disease (ESRD). Of these patients, about 415,000 receive chronic hemodialysis. This population is at risk for increased rates of hospitalization, and increased morbidity and mortality due to the decline in kidney function and associated complications. Moreover, these patients often live with other co-morbidities associated with chronic kidney disease such as anemia and hypertension. Pharmacist involvement in ESRD pharmacotherapy has demonstrated improvements in patients' medication knowledge, quality of life and disease-oriented outcomes. Still, there is limited data on patient-oriented outcomes such as rates of hospitalization, length of stay and patient satisfaction assessments. The aim of this study is to identify the impact on patient satisfaction when medication reconciliation and discharge medication education counseling are provided by a student pharmacist.

Methods

This is a prospective, match cohort study involving patients between the ages of 18 and 80 admitted to Oakwood Hospital and Medical Center. Hospitalized patients identified with ESRD receiving hemodialysis will be consented for inclusion in this study. Patients must have at least one of the following co-morbidities managed with medications: diabetes mellitus, anemia, hypertension, or mineral bone disease. Patients will be randomized to receive the student pharmacist medication reconciliation and discharge education service or standard of care provided by physicians and nursing staff at admission and discharge. The Satisfaction with Information about Medicines Scale (SIMS) will be administered to patients at 10 days post-discharge to assess satisfaction with the

medication information received at discharge. The SIMS survey will specifically assess medication education provided on nephrology-related disease states. The study will be submitted for approval to the Wayne State Institutional Review Board prior to data collection. To maintain patient confidentiality, all patient identifiers will be removed from data collection.

Abstract No. 57 (Student_Graduate)

Title

Older Adult Satisfaction with P3 Community IPPE Student Pharmacists During an Interprofessional Older Adult Home Visit

Affiliations

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Authors

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Abstract

Objectives: To determine older adult satisfaction with the Medication Therapy Management assignment of the Interprofessional Older Adult Home Visit (IPTV) . The IPTV is a component of the P3 Community Introductory Pharmacy Practice Experiences (IPPE)

Methodology: P3 student pharmacists performed medication therapy management (MTM) reviews with older adults over two visits. During visit 1, P3s obtained a comprehensive medication history from the older adult. P3s

identified and resolved drug related problems (DRP), created medication calendars, finalized the recommendation patient letter with a pharmacy preceptor, and then explained the materials to the older adult on visit 2. A satisfaction survey was created after reviewing other pharmacy service satisfaction surveys. The survey covered P3 professionalism, recommendation quality, reasons older adults could not implement the recommendations, and demographics. Student researchers gave the older adults the survey during an interview to find out the older adult's acceptance level of the P3's recommendations. IRB approval was granted. Descriptive statistics were used to summarize data.

Results: Response rate was 56% (35 responders out of a possible 62). The older adults were 76.7 + 6.5 years old (range 68-94) with 70% women, 63% white, and 31% black. All older adults thought the student pharmacists were professional, competent, and showed genuine interest in their health and were satisfied with the MTM review. The older adults felt the MTM review improved health (91%), quality of life (80%), and medication knowledge (97%) ... and decreased medication costs (53%). 37% of the older adults implemented all of their recommendations. Main reasons for not implementing recommendations were doctor visit pending (18%) and doctor did not agree for reasons unknown (18%). 77% of older adults would like a student pharmacist on their health care team.

Conclusions: Older adults found value and health benefits from student pharmacist MTM recommendations.

Abstract No. 58 ()

Title

Health Care Student Learning About Interprofessional Older Adult Home Care

Affiliations

1Pharmacy Practice, Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences, 2BSW/MSW programs, Wayne State University, School of Social Work, 3Co-Curricular Programs, Wayne State University, School of Medicine

Authors

Jordan A. Masse¹, Cassandra Bowers², Jennifer Mendez³, Carol A Bugdalski-Stutrud¹, Geralynn B. Smith¹, Mary Beth O'Connell¹

Abstract

Objectives:

Qualify and quantify student learning from an interprofessional team visit with an older adult in the community.

Methods:

621 students (74 IPPE year 2 and 67 IPPE year 3 pharmacy, 267 second year medical, 87 BSW and 126 MSW social work) were grouped into 2 or 3 discipline teams to interview an older adult. Each student did discipline specific assessments. Student participants completed a post visit learning survey composed of 6 demographic, 17 Likert-based, and 4 open-ended questions. IRB approval received. This study analyzed the "List 3 facts you learned about interprofessional older adult care" question. One investigator created initial codes for each student reflection. Three investigators created focused codes from the initial codes. Focused codes were categorized into themes. Focused codes and themes were quantified. Data were summarized for all students.

Results:

This experience was considered worthwhile by 76% of students. Each student reflection

generated 1 to 7 initial codes, resulting in 1620 total initial codes. Eight themes (with subcategories) emerged: Team value (7), Team structure/process (5), Team function (4), Tools (7), Professionals (7), Older adult (10), Communication/Interviewing skills (3), and Learning (4). In the area of team value, students commented on team importance, additional information generated, better assessments, outcomes, and a more holistic approach. In terms of team structure and function, students commented on the importance of coordination, cooperation, and professional contributions, and issues relating to decision making and responsibilities. Although students found overlap in assessments and roles, they still recognized the unique contribution of each discipline. Communication was considered important, which results in improved interprofessional dialogue and patient care. Students felt the older adults were appreciative and benefited from this experience.

Implications/Conclusions:

Most students evaluated the team visits with an older adult as educational and worthwhile. Students increased their appreciation for team care and understanding of requirements for effective team functioning.

Abstract No. 59 (Student_Graduate)

Title

Implementation of MTM Recommendations by Community IPPE P3 Student Pharmacists Post Older Adult Interprofessional Team Home Visit

Affiliations

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Abstract

Objectives: Quantify implementation of medication therapy management (MTM) recommendations made by P3 student pharmacists for older adults

Methodology: During the first interprofessional team visit (IPTV), P3s obtained a comprehensive medication history from the older adult. With preceptor review and approval, P3s identified and resolved drug related problems (DRP), created medication calendars, and finalized the patient recommendation letter. During visit 2 the P3 explained the materials and recommendations to the older adult. Six older adults had two team visits. A cover letter and information sheet were sent to older adults with an option to withdraw from study. Two weeks later, student investigators contacted 35 older adults to schedule interviews. Student investigators captured implementation data for each DRP recommendation. Each DRP was assigned a pharmaceutical care category, product type, and therapeutic class (based on AHFS categories). Each older adult received a \$10 gift card. Nonparametric statistics were used to summarize data. IRB approved this research.

Results: Of the 35 older adults, 367 DRPs recommendations (9.0 + 6.4 per older adult visit ... range 2-38) were made with 60% implemented. Of the 35 older adults interviewed, 57% discussed DRP recommendations with their doctor, the rest discussed with family, friends, or did not discuss at all. DRPs types (acceptance rates) were 91 benefits/ADRs (25%), 72 monitoring (20%), 60 lifestyle management (16%), 58 medication adherence issues (16%), 46 immunizations (13%), 21 cost lowering strategies (6%), and 18 patient education (5%). Medication DRP types (acceptance rates) were 130 prescriptions (35%), 48 vaccinations (13%), 24 nutritional supplements (7%), and 22 OTC (6%). Select

medication DRP categories (acceptance rate) were 37 cardiovascular (10%), 32 CNS (9%), 15 hormones (4%), 12 GI (3%), and 12 electrolytes (3%).

Conclusion: Student pharmacists contributed to older adult health by identifying and recommending solutions to DRPs which were highly accepted by older adults.

Abstract No. 60 (Student_Graduate)

Title

Doxorubicin-loaded PLGA nanoparticles: preparation, characterization and in vitro evaluation

Affiliations

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Authors

Amer Alali ... Jesse Veenstra ... Emilia Czyszczon ... Wei-Zen Wei, PhD ... Joshua Reineke PhD.

Abstract

Doxorubicin is extensively used in anticancer therapy and known for inducing immunogenic cancer cell death. However, it is highly hydrophilic, has short half-life, and its use is associated with severe cardiotoxicity. Encapsulation of doxorubicin within PLGA NPs will protect the patient from toxic effects associated with high-concentration bolus doses because the NPs will tend to accumulate in tumor tissue much more than they do in normal tissues (EPR effect) and release the drug in a controlled manner so that its available concentration is maintained within therapeutic levels - above the minimum effective concentration but below the toxic concentration

- for longer periods of time. To improve its applicability in cancer therapy and enhance its immunomodulatory effect, we encapsulated doxorubicin in poly(lactic-co-glycolide) (PLGA) (biodegradable polymer) nanoparticles, to achieve controlled release at the tumor sites. Doxorubicin-loaded NPs were prepared by a phase inversion method. These doxorubicin-loaded NPs were characterized for particle size, zeta potential, drug encapsulation and drug release. Electron microscopy of the nanoparticles was used to confirm particle size and surface morphology. The in vitro antitumor efficacy of doxorubicin-loaded NPs was evaluated in D2F2 mouse mammary carcinoma cells.

Abstract No. 61 (Student_Graduate)

Title

Impact of Formal Supports on Family Quality of Life for Caregivers of Persons with Dementia

Affiliations

Occupational Therapy Program, Department of Health Care Sciences, Wayne State University

Authors

Alisha Cole, OTS ... Sarah Czech, OTS ... Fahd Saleh, OTS ... Craig Skonieski, OTS ... Molly Varon, OTS ... Rosanne DiZazzo-Miller, DrOT, OTRL, CDP ... Preethy Samuel, PhD, OTRL

Abstract

Background Significance: Eighty percent of care for persons with dementia is provided by unpaid family members, a contribution to the nation valued at over \$210 billion. Due to the progressive deterioration of cognition, people with dementia become a risk for themselves and are usually unable to live alone safely. The objective of this study is to examine the needs of family caregivers of persons with dementia and examine how it influences their family quality of

life. Methods: A recently adapted comprehensive measure of Family Quality of Life (FQOLS-2011) was used to conduct semi-structured interviews with 12 family caregivers of persons with dementia in Michigan. The cross-sectional data collected from this sample of convenience was analyzed at the univariate and bivariate levels using SPSS 20.0, to test the hypothesis that service support has a significant impact on overall FQOL. Results: About 33% of our participants reported that they were in need of services and about 17% were unsure if they needed more support services, while the remaining 50% reported that they did not have any unmet services. The most common needs were related to transportation, respite care, day programs/activities, and support groups. Correlation analysis revealed that attainment ($r = 0.89$, $p < 0.01$) and satisfaction ($r = 0.74$, $p < 0.01$) of service support was significantly correlated to overall FQOL. Conclusions: In order to help improve the quality of life of persons with dementia, we must understand the need and types of supports desired by their caregivers. Our findings show that the resources spent on developing services to educate and empower family caregivers has the potential to significantly improve the quality of life of the entire family of the person with dementia.

Abstract No. 62 (Student_Graduate)

Title

Single high dose administration of methamphetamine increases dopamine transporter, dopamine D2 receptor, and parkin levels in rat striatum

Affiliations

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Authors

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MOSZCZYNSKA PhD

Abstract

Methamphetamine (METH) is a widely abused psychostimulant with neurotoxic effects. In recent years, there has been an increase in METH-related emergency room visits which creates a burden on the medical system and leaves a need for better understanding of the mechanisms of METH toxicity. METH toxicity is characterized by damage to both dopaminergic (DAergic) and serotonergic (5HTergic) terminals in the striatum, a small region located in the interior regions of cerebral hemispheres. METH toxicity in the striatum is mediated by the dopamine transporter (DAT), a membrane bound protein responsible for dopamine (DA) uptake, and DA receptors. METH is a substrate for DAT. The interaction between METH and DAT causes uptake of the drug with subsequent DA-efflux. In vitro, DAT is quickly mobilized to the membrane in the presence of METH. DAT membrane levels are regulated by protein-protein interactions with dopamine D2 receptor (D2R) and parkin, an ubiquitin-protein E3 ligase. In vivo, binge METH inhibits DAT in a manner dependent on D2R activation but does not appear to change DAT membrane expression. It is not known whether parkin interacts with the DAT in vivo. Together, these findings suggest that the trafficking of DAT may play a role in the early METH response. However, this effect has not been demonstrated in vivo and the effect of METH on D2R and parkin trafficking is still not clear. The aim of the current investigation was to assess 1) METH neurotoxicity in the striatum, 2) DAT, D2R, and parkin levels in striatal synaptosomes, and 3) changes in protein ubiquitination following single bolus administration of METH. Adult male Sprague-Dawley rats were administered METH intravenously and striatal tissue was harvested at various time-points. Striatal synaptosomes were then assessed for catecholamine content using

HPLC at 7 days post-METH and protein levels using western blot analysis at 5min, 15min, 30min, 1hr, 4hr, and 24hr post-METH. Our results show that METH facilitates very rapid increase in the levels of DAT, D2R and parkin in the striatum. The levels of all three proteins remained elevated for an extended period of time, returning to near basal levels 24 hours post METH. Concurrently, total level of both mono/poly ubiquitinated proteins decreased at the designated time points after METH injection. Furthermore, significant reductions in both serotonin and its metabolite were observed in 7 days following METH administration while DA levels were unaffected. Our results suggest that a single high-dose of METH is sufficient to rapidly mobilize DAT to the synaptic membrane and cause long term reduction in 5HTergic terminals. Whether DAT trafficking is regulated by parkin and/or D2R is under investigation.

Abstract No. 63 (Student_Undergrad)

Title

Factors that Influence Treatment Outcomes in Patients with Clostridium Difficile Infection

Affiliations

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Authors

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Lama Hsaiky, PharmD ... Raymond Cha,
PharmD

Abstract

Background: Clostridium difficile infection (CDI) is an aggressive nosocomial infection that is responsible for approximately 1 of 5 cases of antibiotic-associated diarrhea. Treatment of

more serious CDI's have become challenging. Many factors have been identified that influence the risk of developing CDI, however, knowledge of their impact on treatment outcomes is limited.

Methods: In this observational study, patients > 18yo with confirmed CDI within 48h and receiving CDI therapy for >72h was identified at Oakwood Hospital and Medical Center from 2009-2012. Patients were analyzed for their various characteristics including: demographics, baseline and changing renal function, CDI presentation, treatment (drug selections, duration of therapy, surgical intervention), concomitant medication use, comorbidities, CDI history, and hospital service. Multiple regression was used to correlate patient characteristics to outcome measures including length of stay (LOS), CDI resolution and recurrence.

Results: Preliminary results of 33 patients are characterized by a median age of 82 and equal distribution of male to female. 27% of subjects had prior history of CDI. 33% of subjects received combination therapy. 21% of subjects had severe category CDI and 27% received other antimicrobials during CDI therapy. Overall, 97% of subjects experienced clinical success while 1 patient died. Mean length of stay was 17±11 days. Factor assessment reveals disease severity, CDI history and the use of concomitant antimicrobials independently predicts outcome of CDI treatment.

Conclusion: Preliminary results suggest that patients with prior CDI history and the use of concomitant antimicrobials may have a higher risk for prolonged length of stay and treatment. The importance of prudent antimicrobial stewardship is emphasized. Additional analyses of a larger cohort is forthcoming.

Abstract No. 64 (Post_Doctoral_Fellow)

Title

Parkin - A Novel Therapeutic Target for Methamphetamine Neurotoxicity?

Affiliations

Department of Pharmaceutical Sciences, EACPHS

Authors

Bin Liu and Anna Moszczynska

Abstract

Addiction to stimulant drugs such as methamphetamine (METH) has a huge impact on the health and well-being of a large number of individuals and imposes a significant burden on the health care system. Currently, there is no treatment available for METH neurotoxicity. The ubiquitin-proteasome system (UPS) is an intracellular protein degradation system which is responsible for the majority of protein turnover within the cell. Parkin, an E3 ubiquitin-protein ligase in the UPS, facilitates the degradation of misfolded and damaged proteins covalently tagged with ubiquitin. We reported that parkin function is decreased by METH, which suggests the deficits in parkin may increase the neurotoxicity of METH to dopaminergic terminals. The mechanisms underlying this parkin effects in METH neurotoxicity may be due to the decreased degradation of misfolded or damaged proteins, such as abnormal α ... -synuclein. The objectives of this study were to investigate 1) whether an upregulation of parkin levels would protect against METH-induced neurotoxicity in the dopaminergic system, 2) whether the parkin effect is related to the formation of intracellular α ... -synuclein inclusions, and 3) the role of parkin in post-translational regulation of α ... -synuclein, such as phosphorylation. The overexpression of parkin was induced by microinjecting parkin-containing recombinant adeno-associated virus 2/6 (rAAV 2/6) transfer vector (AAV-parkin)

into the substantia nigra pars compacta (SNpc) on one side of the rat brain. Twenty one days later, rats were treated with METH (7.5 mg/kg x 4, i.p.) or saline (1 ml/kg). Rats were sacrificed for Western blot or Immunohistochemistry analysis 7 days later. Hemispheres injected with AAV-parkin showed higher parkin-immunostaining than non-injected hemispheres in both dopaminergic terminals in the striatum and cell bodies in the SNpc. The levels of tyrosine hydroxylase (TH), a dopaminergic marker, were not significantly different between AAV-parkin-injected and non-injected hemispheres. Parkin overexpression attenuated the METH-induced decrease in TH immunoreactivity in the striatum suggesting that parkin protects against METH-induced neurotoxicity. This effect was concomitant with an increase in α ... -synuclein inclusion formation in the striatum suggesting that the intracellular insoluble/non-toxic inclusions may play an important neuroprotective role in METH neurotoxicity. In the SNpc, AAV-parkin microinjection increased the level of pSer129- α ... -synuclein, but not α ... -synuclein, which was accompanied by an increase in ubiquitinated proteins. It suggests that the increased phosphorylation state of α ... -synuclein at Ser-129 in SNpc may contribute to the increased α ... -synuclein inclusion formation in the striatum in parkin-overexpressed rats treated with METH. It is concluded that an overexpression of parkin attenuates the damage to striatal DAergic terminals produced by METH, which may result from the α ... -synuclein inclusion formation and increases in pSer129- α ... -synuclein and ubiquitin. These data may assist the development of pharmacological therapies to ameliorate potential neuronal damage due to MA abuse.

Support by NIH DA023085

Abstract No. 65 (Student_Graduate)

Title

Evaluating toxicity of emerging contaminants: Effects of cholinergic agents in Daphnid cardiorespiratory and behavioral assays

Affiliations

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Authors

Bryan Hannan¹, B.S., Maya Zein², M.S., Shawn McElmurry², Ph.D., Donna Kashian³, Ph.D., David Pitts¹, Ph.D.

Abstract

There is increasing concern about chemicals detected in our waters that pose risk to human health and the environment known as "emerging contaminants". Such chemicals are typically detected in low concentrations (ppb), and their mode of action in the environment is not well understood. Advances in the health care system are associated with the development of various types of pharmaceuticals and personal care products (PPCPs). PPCPs are used in large quantities world wide, and are introduced as parent compounds or as metabolites directly to our water systems and the environment. Concern about environmental contamination by these compounds is heightened, especially because they tend to be biologically active at very low concentrations and often occur in water samples as part of a complex mixture of contaminants. PPCPs may affect physiological processes in exposed organisms, and may impair reproductive, endocrine and immune system function. Daphnia are small planktonic invertebrate crustaceans (0.5-5.0mm) commonly used for aquatic toxicity testing because they are a keystone species with a high sensitivity to environmental changes. Daphnia are ideally suited for toxicity studies because of their short

life cycle, large brood sizes, asexual reproduction, and sequenced genome. *Daphnia* have the highest homology to the human genome (~90%) among known arthropod genomes. Two new methods for evaluating the physiological and behavioral effects of PPCPs have been developed by this multidisciplinary team. The hypothesis of a cardiorespiratory study that focuses on individual animal physiology is: *Daphnia* heart rate (HR) is inhibited by endogenously released acetylcholine via muscarinic receptor activation. Individual *Daphnia* (*pulex* or *magna*) are placed in a sealed aquatic chamber and motor responses to drugs are recorded with a digital camera and quantified using image analysis software. Results show that the muscarinic agonist, oxotremorine, and the acetylcholinesterase inhibitor (AChE-I), physostigmine, elicit a concentration-dependent reduction in appendage beat rate (ABR, respiratory function) in *Daphnia pulex*. Oxotremorine and physostigmine have significantly greater effect on ABR than on HR in *Daphnia pulex*. *Daphnia pulex* ABR is more sensitive than *Daphnia magna* ABR to effects of physostigmine. In contrast to the small inhibitory effects on HR in *pulex*, oxotremorine causes a significant concentration-dependent increase in HR in *magna*. In contrast to expectations based on previous studies, *Daphnia magna* HR does not appear to be decreased by ACh. Evidence to date strongly suggests that there is significant cholinergic modulation of ABR in both *pulex* and *magna*. *Daphnia* respiratory function (ABR) is sensitive to AChE-I, and this may be a cause of lethality resulting from AChE-I insecticide exposure. A behavioral study examined multiple freely swimming *Daphnia pulex*. The animals are simultaneously recorded using a digital camera and then the distance traveled, accumulated distance, velocity, acceleration and angular change are then quantified with image analysis software. The hypothesis of the behavioral study is that: emerging contaminants cause sub-lethal changes in behavior that can be detected by optical tracking techniques. Basal, untreated, activity has been quantified into the 5 different variables, and physostigmine is planned to be the first drug challenge examined in this

behavioral assay.

Abstract No. 66 (Student_Undergrad)

Title

"No Texting While Driving in the Motor City": Development of a 'Hands On' Distracted Driver Prevention Program at EACPHS

Affiliations

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Rajiv George - Department of Health Care Sciences, EACPHS ...

Randall Commissaris - Department of Pharmaceutical Sciences, EACPHS

Authors

Amber Martin, Rajiv George, MS and Randall Commissaris, PhD

Abstract

Rationale: Distracted driving is a significant contributor to motor vehicle accidents and distraction-related accident fatalities. Texting while driving is a particularly potent form of distraction, and incidents of texting while driving and accidents relating to texting while driving continue to be on the rise. Educational programming to prevent/reduce texting while driving often has little effect, in part because they (1) lack a hands-on component and (2) do not "connect" sufficiently well with their target audience of younger, texting drivers. The present abstract describes a program currently in development, the "NO Texting While Driving in the Motor City" project. Purpose: This is a hands-on public outreach program designed to increase awareness by young drivers of the problems of texting while driving and thereby reduce the frequency of accidents associated with texting while driving. We hypothesize that hands-on experience with the problem of texting while driving (a simulator), and perhaps seeing real-world friends experiencing the problems of

texting while driving, will be effective in helping young drivers appreciate of the problem of texting while driving. Subjects: All research subjects will be groups (20-30/group) of unpaid volunteers over 18 years of age ... many will be recruited from the population of students at the EACPHS. Experimental Design: Most groups of subjects (except absolute untreated controls) will receive a brief PPT presentation by the project investigators regarding the dangers of texting while driving, including (for some groups) viewing a video of the research investigators texting while driving the simulator. Some groups of subjects will be asked to identify 2-3 students to operate the driving simulator in a 'live' texting while driving experience ... those members of the group who do not drive will watch a live video feed of their classmates driving while texting. For the texting and driving component, subjects will drive the simulator and occasionally be engaged in a text conversation with a Research Assistant. During these drives, the non-driving students in the group will be engaged in a discussion about the driving, particularly how texting affects driving performance of their classmates. Data Collection: After completion of the experiment, all subjects will complete a questionnaire regarding their personal driving experiences (in the real world), their texting experiences in the real world, their perception of how texting affects driving (eyes, hands, concentration), and whether they will advocate against texting while driving among their peers ... Predicted Outcomes: It is predicted that personal experience with the driving simulator will have the most powerful effect on attitudes toward texting while driving. It is further predicted that live-stream viewing a classmate/friend texting while driving will have a greater impact than viewing a video of someone not known to the group. Finally, it is predicted that an educational PPT presentation alone will be only slightly better than no involvement with the program at all.

Abstract No. 67 ()

Title

A Survey of Vaccines and Vaccine-Preventable Diseases Knowledge, Attitudes, Behaviors, and Practices Among Older Adults in Monroe County, Michigan.

Affiliations

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Authors

Jessica Traster, Carolyn Archer, Paul E. Kilgore

Abstract

Introduction: In the United States, healthy older adults and those suffering from a range of chronic conditions are at risk for serious vaccine-preventable infectious diseases, including hepatitis B, herpes zoster (shingles), influenza, pneumonia, and pertussis. Nationally, population coverage rates for adult vaccines remain below targets set by both Healthy People 2010 and 2020, including for older adults. In Michigan, rates for adult immunizations remain below national goals. While several potential barriers exist to limit adult immunizations in Michigan, there is relatively limited data on the state of current knowledge about vaccines and vaccine-preventable diseases among older residents.

Objective: The goal of this survey is to understand current knowledge, attitudes, and practices regarding vaccines and vaccine-preventable diseases among older adults.

Methods: We developed an interviewer-administered survey for adults aged 60 years and older living in Monroe County, Michigan. Participants were identified, recruited and surveyed in senior centers and hospitals located in Monroe (the Monroe Center for Healthy

Aging, Frenchtown Senior Center, and Mercy Memorial Hospital). Participants were surveyed for their knowledge, perceptions and experience with vaccines and vaccine-preventable diseases including hepatitis B, herpes zoster, influenza, pneumonia, and pertussis. In total, this survey will enroll 320 participants. Univariate and stratified data analysis will be performed to compare subgroups among the sample of adults surveyed.

Results: Among 73 participants interviewed to date, 60 (82.1%) were female and 13 (17.8%) were male. Sixty-five (89.0%) were \geq 65 years of age (eight were aged 60-64 years of age) and 67 (91.8%) were non-Hispanic Whites. Overall, 62 (84.9%) participants felt that vaccines were important while 11 (15.1%) were unsure or did not feel vaccines were important. Notably, when asked about individual adult vaccine-preventable diseases (i.e., hepatitis B, herpes zoster, influenza, pneumonia and pertussis), a high percentage (>95% for each vaccine) had heard of the disease. Among all the older adult vaccine-preventable diseases, participants felt most often at risk for influenza (61.6%, n = 45), pneumonia (43.8%, n = 32) and herpes zoster (38.4%, n = 28). These responses also paralleled opinions regarding those vaccines that the older adult participants felt were important to their health. Notably, only 46.6% (n = 34) felt that the Tdap (pertussis) vaccine was important to their health. Among this group of older adults, 63 (86.3%) had received an influenza vaccine in previous years. A similar percentage of participants (61.6%, n = 45) had received a pneumococcal vaccine. A substantially lower percentage of participants had received either the Tdap vaccine (31.5%, n=23) or the herpes zoster vaccine (27.4%, n = 20).

Conclusion: Our survey suggests that there are significant gaps in knowledge among older adults. Important opportunities exist for education, outreach and advocacy about vaccines and vaccine-preventable diseases among older residents in Monroe County, Michigan. Results of this survey will be critical to the design and implementation of future adult

immunization programs in Monroe County and elsewhere in Michigan.

Abstract No. 68 (Student_Graduate)

Title

Learning Assessment of the Peruvian Amazon Study Abroad Program

Affiliations

Wayne State University, College of Pharmacy and Health Sciences (S. Priest and Dr. O'Connell)
Global Awareness Institute (GAI) (Dr. Brodman and Dr. Nemire)

Authors

Shannon Priest, Pharm.D. III
Dr. Mary Beth O'Connell, Pharm.D., BCPS, FASHP, FCCP
Dr. Barbara Brodman, PhD.
Dr. Ruth Nemire, B.S.Ph, Pharm.D., Ed.D.

Abstract

Objective: Assess learning, professional practice, personal growth, and global responsibilities from the "Medicinal Plants and Cultures of the Amazon" program.

Methods: A survey was sent via SurveyMonkey to 59 former student pharmacists who participated in the program between 2003 and 2012. The survey had 8 sections: course preparation (5 questions), logistics (11 questions), learning (11 questions), and immersion (13 questions), personal growth (10 questions), professional practice (11 questions), global awareness (6 questions), and demographics (15 questions). Descriptive statistics were used for data analysis.

Results: Response rate was 54%. Student demographics at time of program were 23.9 + 1.8 years old, 70% women, 33% no prior

international travel, and 23% conversational and 40% some Spanish fluency. The primary reason for participation was immersion in a different culture with 87% listing improving cultural competency as a secondary reason. Although 21 students had initial culture shock, 8 students felt homesick and 5 students had language problems all but one student stated they had the skills needed to deal with program stresses. Learning with an interpreter created a better immersion experience for 93%. Areas of greatest learning were herbal therapy, shamanism and rainforest barriers with slightly less learning about creating medicinal products from herbs and rainforest sustainability. Half improved their counseling on herbal therapy. Almost everyone improved her/his respect and appreciation of alternative health beliefs and felt better equipped to serve patients from other cultures. Many students (63%) have modified their behavior to better preserve the rainforest. This course was ranked as the best in curriculum by 47% and all but 1 actively encouraged other students to participate.

Implications/Conclusions: Students learned and grew from this study abroad program. The program contributed to students' understanding of Peruvian culture, improved professional practice, increased knowledge of global issues and, created greener lifestyles to save the rainforest.

Abstract No. 69 (Student_Graduate)

Title

Assessment of the Adherence to Treatment Guidelines for Discharge Medications for Patients Admitted to the Hospital for COPD Exacerbation

Affiliations

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University (affiliation for Kevin Costa, Emily Fisher, Cassandra Petros and Sheila Wilhelm)

Harper University Hospital (affiliation for Geoffrey Morgan and Sheila Wilhelm)

Authors

Kevin Costa, Pharm D Candidate 2013 ...
Geoffrey Morgan, Pharm.D. ... Emily Fisher
Pharm D Candidate 2013 ... Cassandra Petros
Pharm D Candidate 2014 ... Sheila Wilhelm,
Pharm.D., BCPS

Abstract

Purpose: The purpose of this study is to determine whether patients admitted to the hospital for chronic obstructive pulmonary disease (COPD) exacerbation are properly medically managed based on published guidelines, during transitions of care, specifically when discharged from the hospital. This study will also determine whether proper medication management results in better patient outcomes, assessed by 30 day readmission rate.

Methods: This retrospective chart review has received Institutional Review Board approval and will examine approximately 400 subjects with an ICD 9 code related to COPD (496, Chronic airway obstruction) admitted to Harper University Hospital, Hutzel Women's Hospital, or the Rehabilitation Institute of Michigan between December 2010 and August 2012. Eligible subjects are between 18-89 years old with shortness of breath documented on admission. The data collected for this study includes patient demographic data, medications at admission and discharge, 30-day readmission rate and cause of readmission.

The primary outcome of this study is to determine if medications at discharge were appropriate according to the GOLD guidelines for a patient with a COPD exacerbation. The impact on 30 day readmission will also be assessed. The use of standardized COPD orders during hospitalization will be determined, and assessment of whether use of these orders increase concordance with guidelines and affected length of stay and 30 day readmission rates will be done. This study will also examine

whether there are medications that are commonly omitted or used without an indication. Lastly, the effect of season of the year on COPD management, length of stay and 30 day readmission rates will be reviewed.

Abstract No. 70 (Student_Graduate)

Title

Evaluation of bleeding events in patients on dabigatran therapy

Affiliations

Wayne State University ... Oakwood Hospital and Medical Center

Authors

Sonia Hassan, PharmD Candidate 2013 ... Larry Diamond, PharmD

Abstract

The ACCF/AHA/HRS as well as the CHEST guidelines have been recently updated to include dabigatran as a favored alternative to vitamin k antagonists in atrial fibrillation patients at risk for stroke. However, post-marketing reports have created a concern for increased bleeding events in patients on dabigatran, leading to an FDA medication safety alert for dabigatran. This study aims to determine the incidence of bleeding and characterize patients at risk for bleeding receiving dabigatran therapy.

This is a retrospective cohort study in which patients 18 years or older will be identified using a report generated for patients receiving dabigatran therapy at Oakwood Healthcare System from November 2010 through September 2012. Patient identifiers will be removed from data collection in order to maintain patient confidentiality. Data will be collected regarding patient demographics, past medical history, pertinent lab values, concomitant medication therapy, CHADS-2

scores, and any anticoagulation-associated adverse events. Continuous data will be evaluated using a T-Test while categorical data will be evaluated using a Chi-Squared test. Any bleeding events will be categorized as minor, major, or life threatening in accordance with the scale from the RE-LY trial. Patients included in this analysis that experienced a bleed will be further evaluated by a logistic regression to identify any risk factors correlated with the administration of dabigatran therapy. This study will be submitted to the Wayne State Institutional Review Board for approval prior to data collection.

Abstract No. 71 (Student_Graduate)

Title

Relationships between Clinical Balance Tests and Balance Confidence in Community-Dwelling Older Adults

Affiliations

Physical Therapy Program, Department of Health Care Sciences, Wayne State University

Authors

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Hassan Dabajeh
Elona Koxhaj
Vanita Shukla
Lance Thomas
Susan Talley, PT, DPT
Allon Goldberg, PT, PhD

Abstract

Falls are one of the leading causes of injury-related deaths among individuals 65 years and older. Prevalence of falls in older adults over 65 years of age is approximately 30% annually. The occurrence of falls in the elderly can lead to fear of falling and reduced balance confidence, both leading to activity restriction. Activity restriction can in turn lead to a decline in physical health,

balance and gait problems, muscle weakness, decreased strength, and falls. The purpose of this study was to investigate the relationship between measures of balance confidence and a variety of balance and mobility measures sub-classified into measures of static, dynamic, and mixed balance and function. Research has shown varying results regarding the ability of balance tests to predict falls. The relationship between balance tests and balance confidence/FOF has not been well studied. We hypothesized that dynamic balance measures would be the greatest predictors of balance confidence. A total of 48 community dwelling older adults ages 65 years old or greater participated in the study. The ABC-16 and ABC-6 scales were used to assess balance confidence in the group of participants. Fear of falling was assessed asking all participants to answer yes or no to the question, "Do you have a fear of falling?" All participants took place in 7 different tests to measure their balance ability. The Four Square Step Test was the only purely dynamic balance measure assessed. Three "mixed tests" were conducted utilizing both static and dynamic characteristics ... these included the Maximum Step Length Test, Step Execution Time, and the Five Times Sit-to-Stand test. There were three tests conducted which were purely static in nature these included Postural Sway measured under two separate conditions first with eyes open on foam and also with eyes closed on foam and the Single Leg Stance test. Data analysis was performed using SPSS 18.0. Descriptive statistics were computed for participant characteristics, as well as for all variables assessed. The Kolmogorov-Smirnov test used to assess normality of study variables. To measure the strength of relationships between dependent and independent variables Pearson product-moment correlation coefficient and Spearman's rho were used on parametric and non-parametric data, respectively. Our findings showed that the Four Square Step Test, a dynamic balance measure, was the strongest predictor of balance confidence of the 7 variables assessed. Max Step Length and Step Execution Time, dynamic measures of balance ability, were also correlated with balance confidence. Based on the findings of this study further research should be conducted to determine the use of dynamic

balance interventions as a potential means of improving balance confidence in community-dwelling older adults.

Abstract No. 72 (Student_Undergrad)

Title

A Survey of Vaccine and Vaccine-Preventable Disease Knowledge, Attitudes, Behaviors and Practices Among Hajj Pilgrims: Application of Community-Based Survey Methods in Metropolitan Detroit.

Affiliations

(1)Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan ... (2)ACCESS, Dearborn, Michigan ... (3)Wayne State University College of Liberal Arts and Sciences, Detroit, Michigan.

Authors

Matthew Duprey(1), Adnan Hammad, MD(2), Carolyn Archer(1), Madique Tariq(2), Zainab Alsamarai(3), Paul E. Kilgore, MD, MPH(1)

Abstract

Background: Each year, over two million Muslims complete the Hajj pilgrimage to Saudi Arabia. During Hajj, the spread of vaccine-preventable infectious diseases (e.g., influenza, meningococcal disease) has been well documented. With many pilgrims traveling from the Metro Detroit area, it is important to understand how travel preparations and mass gathering initiatives influence uptake of vaccines. Because Hajj pilgrims constitute an important yet potentially hard to reach population, we developed a community-based strategy for implementation of a vaccine survey among the Arab-American community in Metro Detroit.

Objectives: The aim of this survey is to ascertain the knowledge, attitude, beliefs, and practices of

Metro Detroit Muslims with regards to vaccine preventable diseases. In the process of conducting this survey, we also seek to identify optimal methods for conducting health research among the Arab-American community in the Detroit area.

Methods: To develop this project, we conducted a review of the existing published literature related to health and illness among Hajj pilgrims. In this review, we identified several vaccine-preventable diseases for which Hajj pilgrims may be at risk during their travels. We further surveyed existing travel recommendations published by the US Centers for Disease Control and Prevention (CDC) as well as the Saudi Arabia Ministry of Health. For preparation of this survey and study protocol, sample size estimations were performed and a specialized training program was implemented for bilingual field interviewers.

Results: Methodologically, this survey posed unique challenges. First, the project team developed a survey tool with 88 questions to assess demographic data, vaccine-preventable disease knowledge and attitudes, and Hajj travel plans. To interview Arab-American participants, we canvassed health care providers, community organizations and travel organizations to identify likely Hajj pilgrims in and around the community of Dearborn, Michigan. Because many Hajj pilgrims may have limited experience speaking English, we identified a group of nine experienced bilingual (Arabic/English) health interviewers and provided them with training in the use of the survey tool. For this survey, confirmed pilgrims aged \geq 18 years will be interviewed in clinics, medical centers, homes, community service organizations, and places of worship. To assist with the interview process, a packet of information containing bilingual vaccine information sheets prepared by the US CDC was developed to allow interviewers to better deal with questions that arise.

Conclusion: The multi-cultural nature of populations in the Metropolitan Detroit area present superb opportunities for collaborative community-based research. The methods, survey tools, and research field staff developed for this

project have established a superb multi-disciplinary collaborative research team that is capable of conducting studies in Arab-American populations and developing research programs in other countries with Arabic speaking populations. Preliminary data also suggests that interventions to increase vaccination rates may be warranted.

Abstract No. 73 (Student)

Title

DKA/HHS protocols and guideline adherence: a quasi-experimental study

Affiliations

Oakwood Hospital & Medical Center, Wayne State University

Authors

Sin-Ling Jennings, David Wilpula

Abstract

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the two most serious acute complications of diabetes, and can lead to death in patients. Both crises also cause a heavy burden on health care costs and hospital admissions. Successful outcomes require prompt treatment and close monitoring. A recent consensus statement by the American Diabetes Association (ADA) outlines the evidence-based management for DKA and HHS. Studies have shown that DKA and HHS protocols can help in managing patients in these crises more efficiently.

In this quasi-experimental study, we assess the adherence to guidelines in a teaching hospital before and after implementation of DKA/HHS protocols. Adult patients who were admitted to the hospital with DKA or HHS diagnosis will be reviewed from the hospital electronic medical record without informed

consent. Our target sample size is 50-60 subjects comparing a pre-protocol arm (historical control) and a post protocol arm (treatment group). Study endpoints include a mix of outcomes measures (rate of blood glucose correction, hypoglycemia, hypokalemia; and time to resolution of anion gap) and process measures (appropriate fluid resuscitation, monitoring of glucose and potassium, KCl supplementation, insulin starting doses, etc.). Statistical analysis will be carried out using chi square tests for discrete variables and student's t-tests for continuous variables. This study will be submitted to the Wayne State Institutional Review Board for approval.

Abstract No. 74 (Student)

Title

Evaluation of the Mechanism of Synergy Between Trimethoprim/Sulfamethoxazole (TMP/SMX) and Daptomycin (DAP) Against Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Affiliations

Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI

Authors

Siddikur M. Rahman, Adam P. Szeliga, Brian J. Werth, Michael J. Rybak

Abstract

Background:

Daptomycin (DAP) is a cyclic lipopeptide that exerts its bactericidal activity against gram-positive organisms by binding to and inserting into bacterial membranes, leading to rapid membrane depolarization and subsequent deregulation of cellular functions, such as DNA, RNA, and protein synthesis. Due to the emergence of MRSA strains that are DAP non-

susceptible (NS), several studies have been performed to analyze the efficacy of various novel combinations with daptomycin against infections caused by these strains. The combination regimen of DAP and trimethoprim/sulfamethoxazole (TMP/SMX) demonstrated very promising data however it is unclear why this combination is synergistic. Therefore we evaluated this novel combination regimen to investigate the potential mechanism(s) of synergy and to determine which component of TMP/SMX is responsible for enhancing DAP's activity.

Methods: 4 clinical MRSA isolates were utilized for daptomycin (DAP) and TMP/SMX activity assessment experiments. Time kill curve (TKC) experiments were completed for all the strains at 0.5 x minimum inhibitory concentration against different combinations of TMP/SMX and DAP to evaluate for synergy. Potassium efflux assays, based on the mechanism of action of DAP, were also done on all 4 strains to determine if DAP activity was enhanced by this combination.

Results:

TKC demonstrated synergy with the combination of DAP + TMP/SMX against the TMP/SMX susceptible strains but not against the TMP/SMX resistant strains indicating a folate mediated pathway is involved in the mechanism of synergy. The potassium efflux assays revealed that there was no increase in K⁺ efflux in cells pretreated with TMP compared to DAP alone indicating that TMP/SMX does not enhance DAP mediated membrane depolarization.

Conclusion:

The precise mechanism of synergy between TMP/SMX and DAP is still unknown. Nevertheless we have demonstrated that the synergy between TMP/SMX and DAP is related to inhibition of folate biosynthesis that does not ultimately lead to an increase in DAP mediated membrane depolarization. Further research is warranted to determine the mechanism(s) of synergy between these agents.

Abstract No. 75 (Student; Late abstract; not in the printed book)

Title

RELIABILITY OF THE V1 ALLSPORT VERSUS THE GAITRITE SYSTEM IN AMPUTEE PATIENTS: A PRELIMINARY STUDY

Affiliations

Wayne State University, Detroit, MI.

Authors

Qaqish R, Taufiq A, Truss A, Reid K

Abstract

INTRODUCTION: Individuals with lower limb amputations who wear a prosthesis often present with gait abnormalities which can lead to increased pain, decreased walking endurance, difficulty with stair negotiation and navigating unfamiliar walking surfaces. To address these risks and understand how deviations in walking patterns influence functional mobility, it is necessary to conduct clinical gait assessments. Velocity and step length were the gait parameters analyzed in this study using the GAITRite® system and the V1 Allsport (V1); video analysis software. The purpose of this study is to determine the validity of V1 Allsport (V1) system by comparing its performance in measuring gait parameters against the GAITRite® system.

METHODS: Seven participants who met the inclusion criteria of the study were recruited from Wright and Filippis facility in Rochester Hills, MI. Participants were asked to walk over the GAITRite® instrumented walkway at a self selected walking speed while being video taped simultaneously with the V1 All sport. Differences between the GAITRite® and V1 were calculated via a percent error for both step length and gait speed. A Bland Altman Plot was created to graphically compare the differences in

measures between the GAITRite®, and the V1 All sport system. Intraclass correlation coefficient (ICC) was performed using the (2,1) method for repeated measures and (2,k) for mean step length and velocity .

RESULTS: Upon comparing step length between the two systems, the V1 shows good agreement between step length measures made by V1 Allsport and GAITRite® systems, apart from outliers having either a shorter or longer **step lengths. Upon comparing velocity, there** was a moderate agreement between gait speed measures made by the V1 Allsport and the GAITRite®, however in subjects with faster gait speeds the agreements were poorer. ICC indicates that the mean length for step 1 and 2, and the mean comparison between the V1 and GAITRite® present strong positive correlations.

DISCUSSION: This information is useful to physical therapists who can use the V1 clinically to conduct gait assessments by using video recordings to analyze patient deficits. These preliminary results suggest that the V1 may be a valid tool to assess spatiotemporal parameters in addition to functional deficits. ICC indicates that the mean length for step 1 and 2, and the mean comparison between the V1 and GAITRite® present strong positive correlations.

CONCLUSION: Future studies will benefit from a larger sample size and syncing the V1 to the GAITRite® system using a time stamp to accurately match the data collected by the two systems.

ACKNOWLEDGMENTS: Appreciation is expressed to all participants in this study

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