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EUGENE APPLEBAUM
COLLEGE OF PHARMACY
AND HEALTH SCIENCES

8th Annual Research Forum

2011



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8th Annual Research Forum 2011

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Agenda:

8:30 AM – 9:30 AM	Poster Setup
9:30 AM – 11:00 AM	Student Poster Judging
11:00 AM	Welcome: Lloyd Y. Young, Pharm. D., Dean
11:15 AM	Introduction to Speaker: Deepak K. Bhalla, Ph. D Associate Dean for Research
11:15 AM - 12:00 PM	Key Note Speaker: William H. Herman, M.D., M.P.H. “The Cost-effectiveness of Interventions in Health and Medicine”
12:00 PM	Faculty Research Recognition and Student Poster Awards: Dean Lloyd Y. Young
12:30 PM	Lunch
12:30 PM – 3:00 PM	Poster Display and Presentation

Key Note Speaker, William H. Herman, M.D., M.P.H.



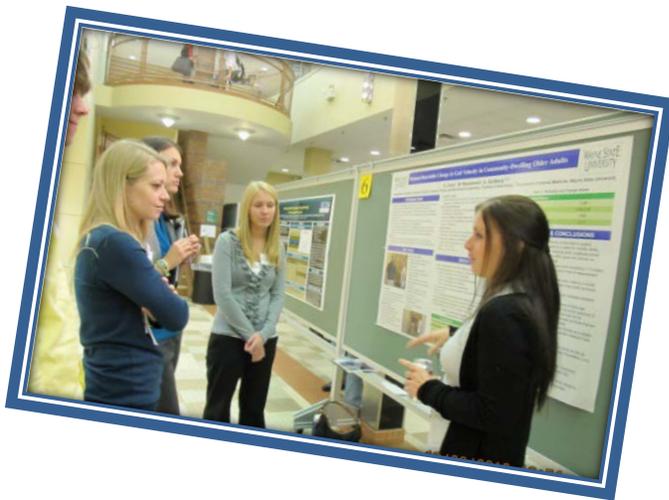
William Hudson Herman, MD, MPH. is an internationally recognized scientist and an expert in diabetes research. He received his BS in chemistry at Yale University, his MD at Boston University and MPH in epidemiology at the University of Michigan. Dr. Herman currently holds the titles of Stefan S. Fajans/Glaxo SmithKline Professor of Diabetes, Internal Medicine, Professor of Medicine and Epidemiology and the Director of Michigan Diabetes Research and Training Center at the University of Michigan. He has contributed enormously to various aspects of diabetes research, including complications in type 1 diabetes, prevention of type 2 diabetes, diabetes care in managed care, diabetes epidemiology and clinical economics.

Dr Herman has held several appointments and distinguished positions in academia and health care sector. He has served on the Editorial Boards of four prestigious journals of Diabetes and on numerous Scientific committees. He has also received several

awards for his contributions to the research in Diabetes. These include U.S. Public Health Service Commendation Medal, U.S. Public Health Service Commissioned Officer Award, American Diabetes Association Charles H. Best Medal for Distinguished Service, American Diabetes Association Award for developing Arab American coalition, Egyptian Diabetes Association Medal, American Diabetes Association Kelly West Award and Pfizer Visiting Professorship Award.

Dr. Herman is an active researcher with an outstanding track record of research funding from NIH and other institutions. He has published over 250 papers and 30 book chapters. He has also presented close to 200 invited lectures. These invitations to present his work reflect on his international stature and high regards for his research.

Poster Presentations



Abstract No. 1 (Poster)

Title

Intersession Reliability of the EMG Amplitude During Incremental Cycle Ergometry: Quadriceps Femoris

Affiliations

¹Integrative Physiology of Exercise Laboratory, ²Mobility Research Laboratory, and ³Institute of Gerontology, Wayne State University

Authors

L. Travis¹, S. Arthmire¹, A. Baig¹, A. Goldberg^{2,3}, M. H. Malek¹

Abstract

Introduction: The purposes of the current investigation were to determine the: 1) reproducibility of the patterns of responses for electromyographic (EMG) amplitude; and 2) intraclass correlation coefficient (ICC) of the EMG amplitude during three incremental cycle ergometer tests separated by 48 hours.

Methods: Ten men performed incremental cycle ergometry tests to exhaustion on three separate occasions. Surface EMG amplitude was recorded simultaneously from the three superficial quadriceps muscles at each trial.

Results: The results of the polynomial regression indicated that, for >95% of the cases, the best-fit model was the same at each trial for EMG amplitude. The ICC values were high for EMG amplitude indicating excellent reliability.

Discussion: These results indicate that EMG amplitude is a reliable measure of motor unit activation strategy during incremental cycle ergometry.

Abstract No. 2 (Student_Graduate)

Title

Assessment of student pharmacist learning from a multidisciplinary older adult home visit

Affiliations

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Authors

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Abstract

Purpose: To assess achievement of pharmacy experiential goals designed to enhance student learning related to aging, social constructs, patient assessment, physician roles, team care, and home visits from a multidisciplinary team experience with older adults in their homes.

Methods: 83 pairs of a third-year student pharmacist and second-year medical student assessed an older adult in his/her home. Student pharmacists performed a comprehensive medication review, identified drug-related problems, and with a pharmacy preceptor created a recommendation letter and medication calendar, which were given to the older adult. Medical students assessed fall risk and activities of daily living. Student pharmacists completed a post-visit learning survey related to curricular goals. Survey questions were analyzed utilizing descriptive statistics (SPSS v19). Open-ended questions were analyzed using qualitative research techniques, resulting in learning themes.

Results: Sixty-six percent of students reported increased understanding about social influences on medication use. Students thought (> 70% responses) team care was more comprehensive, could improve patient outcomes, and would be important to their professional success. Most students (96%) believed the home visit resulted in additional information that could improve health care delivery. Based on qualitative findings, students learned that older adults were more active, independent, and knowledgeable about their health than expected. They felt the medical students were empathetic toward the older adult and demonstrated positive personality traits, professionalism, and good interviewing skills. Students described multidisciplinary team care as important and provider roles complementary. The home visits were noted to provide an environment more comfortable for the older adult as they were quite amiable, communicative, and receptive to information provided by the team. Most students (86%) indicated the project was worthwhile and would recommend it to other students.

Conclusion: Multidisciplinary training with older adults in a home environment was a good learning opportunity for the students.

Abstract No. 3 (Student_Graduate)

Title

Experiential Value of an Older Adult Medication Assessment Early in the Pharmacy Curriculum

Affiliations

Department of Pharmacy Practice, Wayne State University.

Authors

Kirsten Freitel, Pharm.D., III, Student, Tara C. Rosenthal, Pharm.D., III, Kimberly M. Rutkowski, Pharm.D., III, Student

Abstract

Purpose: To evaluate the learning and appropriateness of an older adult medication review early in the curriculum.

Methods: Older adults visited the college to meet

first-year students who would soon provide their medication review with a pharmacist. The team performed the review at the older adult's independent living residence during spring/summer year one experiential courses (IPPE). The pharmacist gave each older adult a medication calendar and list of recommendations. Three months later, the students visited their older adult to learn about recommendation implementation. After each aspect, students wrote a reflection. Students completed an anonymous learning survey after the program (39% response). Descriptive statistics (SPSS v19) were used to summarize survey data and qualitative research techniques (Atlas.ti v6.2) were used to determine learning themes from the reflections.

Results: Students (\geq ... 73%) felt comfortable speaking with older adults at the social event, were confident in their duties, and thought the follow-up visit was valuable. They felt the medication review was beneficial to the older adult (70%). This experience helped develop communications skills (60%), enhanced understanding of pharmacists' roles in medication management (70%), and expanded medication knowledge (57%). Students thought this project should be continued (57%) and recommended changes. In the reflections, students described learning about older adult lifestyles, health, and medication issues. Students were able to practice and improve skills gained throughout didactic and lab courses (e.g., self-confidence, older adult interviewing). They learned how to prepare a medication calendar. Many students felt the older adults also benefited from the interaction. Drug related problems were identified and resolved throughout the project that might not have been recognized otherwise. Reflection reviews from the social event and 3 month follow-up visit are pending.

Conclusion: Students learned about older adult lifestyles, medication issues and assessment adjustments. The experience will be continued in the curriculum with changes.

Abstract No. 4 (Student_Graduate)

Title

A Multi-Centre Evaluation of the Impact of Drug Shortages in Neurocritical Care (NCCU): Management Strategies and Resource Utilization

Affiliations

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Abstract

Introduction

Drug shortages have been increasing at an alarming rate. Many of these agents have a substantial impact in neurocritical care. As shortages become more common we sought to highlight management strategies, institutional impact, and overall assessment of shortages in NCCU.

Methods

An electronic survey was sent to 62 pharmacy members of the Neurocritical Care Society. This survey assessed resources used to obtain information regarding drug shortages, management strategies, resources required to manage shortages and overall assessment of drug shortages in NCCU.

Results

Of the 43 respondents (69.4% response rate), the majority were located at large (>499 beds), urban

settings (85%) in the Midwest (32.5%) or South (52.5%) and were predominately affiliated with academic institutions (90%) and had dedicated NCCU (90%). The majority of institutions have computerized physician order entry (75%) and greater than 50 pharmacist FTEs (60%). Commonly used resources to identify drug shortages include ASHP website (54.8%), internal drug information services (75%) and buying groups (68.6%). Pharmacists were primarily responsible for identifying drug shortages (93.8%), developing policies/protocols/guidelines (75%) and implementing those policies/protocols/guidelines (93.8%), and identifying therapeutic alternatives (100%). Pharmacists spent, on average, 29.27 hours per month tracking shortages, 19.89 hours per month identifying therapeutic alternatives, and 9.38 hours per month providing in-services to hospital staff. The majority strongly agreed that drug shortages in their NCCU increased institutional burden (81%), increased costs with developing action plan (55%) and purchasing alternative agents (61%), increased frustration regarding these shortages directed towards pharmacy (81%), lack of advanced warning (71%), and lack of information on duration of shortage (52%). Respondents strongly agreed/agreed that shortages changed clinical practice (87%), compromised care (61%), and resulted in secondary drug shortages (74%).

Conclusions

Drug shortages in the NCCU led to increased institutional burden in resources and cost. Additionally many NCCU pharmacists believe drug shortages changed practice and information regarding shortages was not optimal.

Abstract No. 5 ()

Title

A National Survey of Drug Shortages in Neurocritical Care Units (NCCU): Description of Shortages With Commonly Used Agents

Affiliations

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Denise Rhoney, Pharm.D., FCCM, FCCP

Abstract

Introduction

Drug shortages have been increasing at an alarming rate. As shortages become more common we sought to highlight patient safety issues, categorize management and resolution strategies, and identify the impact on clinical practice of neurocritical care.

Methods

An electronic survey was sent to 62 pharmacy members of the Neurocritical Care Society. This survey assessed types of intravenous agent shortages experienced, alternate agents used, and perceived clinical impact, including patient safety and resources.

Results

Of the 43 respondents (69.4% response rate), the

majority were located at large (>499 beds), urban settings (85%) in the Midwest (32.5%) or South (52.5%) and were predominately affiliated with academic institutions (90%) and had dedicated NCCU (90%). Respondents indicated the most common agents in shortage were IV bactrim (84.4%), norepinephrine (78.1%), propofol (75%), and fosphenytoin (75%). In some cases, an agent on shortage was substituted with an alternative agent that was also on shortage ... causality cannot be determined. While adverse events (AE) due to the shortage were not common there were 7 delayed/cancelled procedures due to thiopental, pentobarbital, and propofol shortages. Other AE experienced: near miss with hypertonic saline (n=1), serious AE with norepinephrine (n=1) and fosphenytoin (n=3), and sentinel event with IV bactrim(n=1). The majority of the respondents indicated that each shortage changed current practice and the agent shortages perceived to most commonly compromise patient care were propofol (26.1%), norepinephrine(33.3%), and bactrim (26.9%). Very few institutions ran out of agents except for thiopental (92%), fosphenytoin (54.2%) and bactrim (55,6%) The level of satisfaction for how each shortage was handled was overall satisfied/very satisfied with the exception of the thiopental shortage, wherein 55% of respondents were dissatisfied or extremely dissatisfied. Perceived resource impact for creating an action plan ranged from very low impact (< 3 hours), to very high impact (> 18 hours) with only propofol being designated very high impact by the majority of respondents (30.4%). The perceived length of shortages ranged from less than one to greater than 12 months.

Conclusions

The increasing number of drug shortages occurring in the United States has had a noticeable impact on the practice of neurocritical care.

Abstract No. 6 (Student_Graduate)

Title

MINIMUM DETECTABLE CHANGE FOR COMMON PHYSICAL PERFORMANCE MEASURES IN OLDER ADULTS

Affiliations

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Authors

Martina Chavis¹, Johnny Watkins¹, Tyler Wilson¹, Allon Goldberg PT, PhD^{1,2}

Abstract

INTRODUCTION: Five time sit-to-stand test (FTSST), Timed Up and Go (TUG) and Functional Reach (FR) are tests that measure balance and functional mobility in older adults. It is not known what constitutes real change beyond that attributable to measurement error for many assessment measures commonly used in geriatric clinical practice. Minimum Detectable Change (MDC) is defined as the minimum amount of change that is not due to random variation in measurement, but represents real change in performance across trials. Thus, knowing MDC for FTSST, TUG and FR enables clinicians to establish what constitutes real change beyond that attributable to measurement error. The purpose of this study was to quantify MDC at the 95% confidence level (MDC95) in community-dwelling older adults for FTSST, TUG and FR. **METHODS:** Thirty community-dwelling older adults were recruited from a senior community center in the Metro-Detroit area. Participants were included in the study if they were a community-dwelling older adult aged 60 years or older, and able to stand and walk at least 10 meters without an assistive device. Participants were tested at one testing session with each participant performing two trials for each test. Intraclass correlation coefficients (ICC_{2,1}) and standard deviations (SD) were used to estimate standard error of measurement [SEM=SD x $\sqrt{1 - ICC_{2,1}}$], a measure of absolute reliability. MDC₉₅ was computed as SEM x 1.96 x $\sqrt{2}$. SEM% and MDC₉₅% (SEM and MDC expressed as a percent of mean) were computed to interpret absolute reliability

and evaluate sensitivity of the measures to detect real change in performance. **RESULTS:** Mean values \pm ... SD were: FTSST 14.2 \pm ... 3.9 seconds, TUG 10.3 \pm ... 3.3 seconds, FR 9.3 \pm ... 2.6 inches. The high ICC_{2,1} for FTSST (0.95), TUG (0.97) and FR (0.79) suggest excellent test-retest reliability. Low SEM% for FTSST (6.3%) and TUG (5.8%) is suggestive of low measurement error and excellent absolute reliability. SEM% for FR is higher (12.9%) and suggests higher measurement error and lower absolute reliability. Low MDC₉₅% suggests that FTSST (17.6%) and TUG (16.5%) may be sensitive in detecting change in performance. In contrast, higher MDC₉₅% for FR (35.5%) suggests that FR may be less sensitive in detecting real change in performance. Change values must exceed 2.5 seconds for FTSST, 1.7 seconds for TUG, and 3.3 inches for FR to be considered real change. Change less than those values are considered to be due to measurement error. **DISCUSSION AND CONCLUSION:** FTSST, TUG and FR exhibit excellent relative reliability. Although absolute reliability of FTSST and TUG is excellent, FR exhibits lower absolute reliability. FTSST and TUG appear to be more sensitive than FR in detecting real change in performance of older adults. The change values reported here can be used by clinicians to evaluate the effectiveness of interventions in clinical settings. One can be 95% confident that a change value exceeding 2.5 seconds for FTSST, 1.7 seconds for TUG, and 3.3 inches for FR, is real change.

Abstract No. 7 ()

Title

Bridging for an isolated subtherapeutic INR: an analysis of clinical practice patterns and outcomes from an anticoagulation clinic

Affiliations

1) Department of Pharmacy Practice Wayne State University, 2) Harper University Hospital Department of Pharmacy.

Authors

Jamie Hwang Pharm.D. 2, Jennifer Clemente Pharm.D. 2, Tom Taylor Ph.D. 1, Krishna Sharma Ph.D. 1, Candice Garwood Pharm.D. 1,2

Abstract

Patients with an isolated subtherapeutic INR are often bridged with parenteral agents in clinical practice, yet there are a paucity of data available to support or refute this practice. Therefore, the purpose of this study is to identify the significant predictors of bridging for an isolated subtherapeutic INR and to investigate the benefits and risks of this practice in terms of adverse events.

Methods Our retrospective chart review examined 392 episodes of isolated subtherapeutic INR (Index INR) occurring in 214 patients at a pharmacist-managed anticoagulation clinic. Index INR was defined as a subtherapeutic INR preceded by 2 INRs in range or above range. Each index INR was classified with a low, medium or high risk for thromboembolism (TE) based on indication and patient risk factors according to the American College of Chest Physician Guidelines on Antithrombotic Therapy. These index INR's were subsequently classified as bridged or non-bridged and further categorized by magnitude below target INR: mildly-low (0 to -0.25 INR units), moderately-low (-0.26 to -0.75 INR units), or severely-low (-0.75 INR units). Adverse events were assessed for bleeding 30 days post index INR and thrombosis 90 days post index INR. For statistical analysis, means and standard deviation were used to describe continuous variables. We used generalized estimating equation methods to account for within-subject correlation in multivariate models evaluating predictors of bridging.

Results Study subjects were predominately African American (75%), mean age of 59 years, and had venous thromboembolism (39%), atrial fibrillation (37%) and mechanical heart valves (12%) as indications for warfarin therapy. Out of 392 episodes identified, 63 episodes (16%) were bridged with enoxparin (81%) or fondaparinux (19%). The mean

index INR was 1.77 ± 0.28 for non-bridged and 1.52 ± 0.25 for bridged episodes ($P<0.0001$). The mean difference between the index INR and minimum target INR was -0.3 ± 0.22 and

- 0.60 ± 0.27 for non-bridged and bridged, respectively

($P<0.0001$). Furthermore, index INRs categorized as severely-low (OR 33.98, $P<0.0001$) and moderately-low (OR 6.75, $P<0.0001$) are more likely to be bridged than mildly-low INRs. We found that the high-risk group for TE are more likely to be bridged than the low risk-group (OR 3.02, $P<0.02$). However, the probability of bridging for moderate-risk of TE is not statistically different compared to low-risk (OR 1.55, $P<0.28$). We identified low rates of adverse events in both groups (Table 1).

Conclusion We propose that that the deviation from the target INR to be the most important predictor of bridging for a subtherapeutic INR, followed by being at high-risk for thromboembolism. The thrombosis rate is low for most cases of isolated subtherapeutic INR. Therefore, not bridging may be a safer option with fewer bleeding and bruising events.

Abstract No. 8 ()

Title

Bridging for an isolated subtherapeutic INR: a cost analysis from the patient, provider, payor and society perspective

Affiliations

1. Harper University Hospital Department of Pharmacy
2. Wayne State University Department of Pharmacy Practice

Authors

Jamie Hwang Pharm.D. 1, Candice Garwood Pharm.D. 1,2, Jennifer Clemente Pharm.D. 1, Krishna Sharma Ph.D. 2, Tom Taylor Ph.D. 2

Abstract

Background Patients with an isolated subtherapeutic INR are routinely bridged with parenteral agents in clinical practice despite unknown thrombotic risk. As the decision of whether to bridge has important implications for patients, providers, payers, and society as a whole, we examine the economic implications of bridging from all four perspectives. **Methods** Our retrospective chart review examined 392 episodes of a low INR (index INR), preceded by two INRs within or above target therapeutic range occurring in 214 patients at a pharmacist-managed anticoagulation clinic. All episodes were categorized as bridged or non-bridged. We estimated a total cost for each episode derived from three levels of costs: (1) Direct medical cost, (2) Direct non-medical cost, and (3) Productivity cost. Direct medical costs are associated with the medical resources used in treatment including dispensed medication, lab tests, and clinic visits. Direct non-medical costs include transportation costs

estimated prospectively through a survey. Productivity costs are defined as patient time spent at clinic plus travel time valued by the median hourly wage for full-time workers. We estimated the three levels of costs by the patient, provider, payor and society perspective. For statistical analysis, the total, direct and productivity costs were calculated as repeated measures over individual patients. We used generalized estimation equation (GEE) methods with gamma distributional assumption and log link function to estimate the total, direct medical, and productivity costs per episode attributable to bridging. **Results** The study subjects were predominately African American (75%), mean age of 59 years with venous thromboembolism (39%), atrial fibrillation (37%) and mechanical heart valves (12%) as indications for warfarin therapy. Out of 392 episodes identified, 63 episodes (16%) were bridged with enoxaparin (81%) or fondaparinux (19%). The mean number of syringes of parenteral anticoagulants prescribed was 10.68 ± 7.07 (range 0–40). The mean duration of bridging was 6.6 ± 4.92 days (range 1–28). There were five confirmed anticoagulation related emergency department (ED) visits and four anticoagulation related hospitalizations. All ED and hospitalizations were bleeding related except two hospitalizations were thrombosis related (1 bridged, 1 non-bridged). The mean total cost for the bridged and non-bridged episodes was \$1,046 and \$281, respectively. The total cost, total direct cost (direct medical and direct non-medical), and total productivity cost was significantly higher than the bridged group. Total, direct and productivity incremental cost of bridging was \$767 ($P < 0.001$), \$756 ($P < 0.001$) and \$13 ($P < 0.05$) respectively. **Conclusion** This study demonstrated that bridging for a subtherapeutic INR entails considerable additional costs to both

patients,
clinics, payers, and society.

Abstract No. 9 (Student_Graduate)

Title

Intersession Reliability of the EMG Mean Power Frequency During Incremental Cycle Ergometry: Quadriceps Femoris

Affiliations

¹Integrative Physiology of Exercise Laboratory, ²Mobility Research Laboratory, and ³Institute of Gerontology, Wayne State University

Authors

L. Travis¹, S. Arthmire¹, A. Baig¹, A. Goldberg^{2,3}, M. H. Malek¹

Abstract

Introduction: The purposes of the current investigation were to determine the: 1) reproducibility of the patterns of responses for electromyographic (EMG) mean power frequency (MPF); and 2) intraclass correlation coefficient (ICC) of the EMG MPF during three incremental cycle ergometer tests separated by 48 hours.

Methods: Ten men performed incremental cycle ergometry tests to exhaustion on three separate occasions. Surface EMG MPF was recorded simultaneously from the three superficial quadriceps muscles at each trial.

Results: The results of the polynomial regression indicated that, for the majority of cases, the best-fit model was different at each trial for EMG MPF. In addition, the ICC values were low for EMG MPF indicating poor reliability.

Discussion: These results indicate that EMG MPF is not a reliable measure of motor unit activation strategy during incremental cycle ergometry.

Abstract No. 10 (Student_Graduate)

Title

GAIT PARAMETERS OF 3, 5 AND 7 YEAR OLD CHILDREN AT SLOW, SELF-SELECTED, AND FAST SPEEDS USING THE GAITRITE® SYSTEM.

Affiliations

Physical Therapy Program, Wayne State University, Detroit, MI

Authors

Ashley Ostrowski, SPT
Andrea Konja, SPT
Susan Ann Talley, PT, DPT, MA
Christine L. Carlson, PT, DPT, MA
Sara Pilon, DPT
Shannon Valicevic, DPT

Abstract

INTRODUCTION/CLINICAL RELEVANCE: Gait speed has been shown to influence temporal and spatial parameters of gait, primarily in adults. The purpose of this study was to collect normative data on the temporal and spatial gait parameters of 3, 5 and 7 year old children walking at slow (SL), self-selected (SS), and fast (FW) speeds and to examine differences in gait patterns indicative of gait maturation. Gait characteristics previously associated with gait maturity were collected: gait velocity, step length, single limb support, double support, cadence, and stance duration. Objective measurement of gait is often necessary in physical therapy to make informed clinical decisions and to demonstrate efficacy of interventions. Normative data is necessary for reference in the evaluation process, particularly for parameters critical to maturation of gait. **METHODS:** Fifty-six healthy young children were recruited from 3 urban schools for this repeated measures design. Eleven participants were between the age of 3 and 3.5 years (3YOs) (38.6 + 2.0 mos ... 72.7% female), 24 were between 5 and 5.5 years (5YOs) (61.8 + 1.2 mos ... 58.3% female) and 21 were between 7 and 7.5 years (7YOs) (87 + 1.4 mos ... 47.6% female). The GAITRite® electronic walkway system was used to collect temporal and spatial gait parameters using a portable 5.5m by .9m portable carpet, embedded with pressure sensitive switches for 4.9m. Participants were asked to walk the length of the mat, plus 2 m at

either end to account for acceleration/deceleration. One practice and 3 walks at each speed were completed. Based on pilot trials, SS speed was always tested last. The order of the FW and SL speed trials were alternated in blocks to minimize an ordering effect. Scripted instructions were used for all children. Alpha was set at .05. RESULTS: There was a significant difference in gait speed between all age groups at the FW speed and between the 3YO group as compared to both the 5YO and 7YO groups. The FW gait speed increased with age. There was no significant difference in gait speed at the SL speed. Cadence was significantly slower in the 7YOs compared to the 3YOs for SS and SL speeds. There was no significant difference in cadence at the FW speed. Step length was significantly different between all groups at the SS and FW speeds, increasing with age, and between the 3YOs compared to both the 5YOs and 7YOs during SL walk. Single leg support was significantly longer for 7YOs compared to 3YOs at both SS and SL speeds. Stance time was significantly longer for 7YOs compared to 3YOs only during the SL walks. DISCUSSION: Gait velocity was most impacted by age at the FW speed. At SL speed there was no difference in gait velocity between groups yet significant differences in other parameters, primarily between the 3YOs and 7YOs. Step length differentiated between all three groups at FW and SS speeds. CONCLUSIONS: The data suggests that control of single limb support, cadence and stance time may contribute to increasing gait maturity.

Carol Bugdalski Stutrud, R.Ph, FAPhA
Jennifer Mendez, Ph.D.
Nelia Afonso, M.D.

Abstract

Objective: To assess the learning of second-year student pharmacist and first-year medical student teams in home visits to older adults living independently. The P2s evaluated the older adult's ability to interpret prescription bottle information, learned about issues influencing medication use, and discussed social constructs on health. This interdisciplinary project included pharmacy, medical and social work students. This activity was a component of the P2s' IPPEs

Methods. Training for all students included a team building presentation. Additional training for P2s included presentations on social constructs affecting older adults and how to use the assessment tools, and review of posted written materials. Written summaries of the preparatory activities were posted in their e-portfolios. Post-visit, P2s reported blinded medication and social construct assessments on Blackboard, and posted un-blinded summary reflections in their e-portfolios. All students completed a blinded Post-Home Survey on Blackboard. P2s completed two visits with different older adults and medical students. P2 second entry in e-portfolio is a comparison of the visits. Formal analysis of this data is to be completed by July 2011.

Results: Initial review of the P2 e-portfolios indicates value of working with medical students as a team in interviewing older adults in their homes and the educational importance of information provided. When all second visits are completed, survey and assessment data will be analyzed.

Conclusion: Preliminary information indicates P2s interviewing an older adult living independently with a medical student is a valuable educational activity. If final analysis supports this, the program will continue as a component of the P2 IPPE.

Abstract No. 11 (Faculty)

Title

Second-Year Students Participation in Interdisciplinary Older Adult Home Visits as a Component of P2 IPPE

Affiliations

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Authors

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Geraldyn B. Smith, MS
Mary Beth O'Connell, Pharm.D., BCPS, FASHP, FCCP

Abstract No. 12 (Faculty)

Title

TOBACCO SMOKE MODULATES THE PULMONARY AND CNS EFFECTS OF OZONE INHALATION IN RATS

Affiliations

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Authors

Bhoopalan, Vanitha¹ Shah, Mrudang M.^{1,3} Thomas, David M.^{1,3} Han, Sung-Gu² and Bhalla, Deepak K.¹

Abstract

Ozone (O₃), an oxidant air pollutant, and tobacco smoke (TS) are known risk factors in the development of lung injury and chronic disease. While the independent toxicity of these pollutants has been widely studied, their interactive effects are poorly defined. This study was performed to determine if sequential exposures of rats to O₃ and TS will influence the toxic responses of O₃ in the lungs and the brain. Adult Sprague Dawley (SD) male rats were exposed for a single 3 hr period to O₃, TS or O₃ plus TS in sequence. In all, 3 exposure groups were evaluated: 1) Air (control), 2) O₃, 3) O₃ followed by TS (O₃/TS). 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 the control, reflecting the inflammatory and cytotoxic effects of O₃. However, a subsequent exposure to TS attenuated PMN infiltration into the airspaces for recovery in the BAL of the O₃/TS group. A similar reduction was also observed for BAL protein in the O₃/TS group, but it was not significant. Since O₃ also induces deleterious effects in the brain, including the nigrostriatal pathway and because the dopaminergic cells of this region are thought to be hypersensitive to oxidative stress, we measured striatal dopamine levels in the O₃ and O₃/TS groups by HPLC with electrochemical detection. Data revealed O₃ reduced striatal dopamine content, while the subsequent TS exposure afforded a nonsignificant protection. Overall, the results show that the toxicity

of O₃ in the lung and brain are modulated by exposure to TS. The results are contrary to the synergistic toxicity predicted for TS and O₃, and are comparable to the attenuated responses following sequential exposures to carbon nanotubes and O₃ reported in our previous studies. Supported in part by funding from OVPR-WSU, NIDA and VA.

Abstract No. 13 (Student_Graduate)

Title

Effectiveness of student pharmacist interventions in antimicrobial stewardship evaluated through intravenous to oral medication interchange in hospitalized patients

Affiliations

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Detroit Receiving Hospital

Authors

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Anthony Jaworski, Pharm.D. Candidate 2013
Dr. Ryan Mynatt, Pharm.D.
Dr. Michael Rybak, Pharm.D., M.P.H.

Abstract

Purpose: The purpose of this study was to evaluate whether student pharmacists could have a significant impact on IV to PO interchanges by actively intervening on PO eligible patients. Many benefits are associated with transitioning patients to oral therapy early in their treatment course. Some of these benefits include shorter length of hospital stay, fewer catheter related infections and infusion related adverse events, increased patient comfort and decreased dependence on caretakers. In addition to patient benefits, there is also a decreased cost for drug preparation and administration with oral therapy.

Methods: Patients were screened using an electronic data capture system. Identified patients were evaluated for PO eligibility based on the Detroit Medical Center IV to PO protocol. Student pharmacists intervened on each eligible patient by calling the physician caring for them and

recommending transition to oral therapy. The data collected included the number of interventions accepted and declined, the number of patients identified who did not meet eligibility criteria, and the length of therapy (used to calculate cost savings).

Results: 261 patients were evaluated and 224 were PO eligible. Of this 224, 68 were intervened on leading to 56 accepted and 12 declined recommendations. The other 156 eligible patients were either changed to oral therapy or had their therapy discontinued before the student pharmacists were able to intervene. The total cost savings for the study period was between \$990.50 and \$1546.69.

Conclusions: 82.4% of the student pharmacist interventions were accepted compared to 61.4% and 82.6% in other studies. Based on our data, the annual cost savings is projected to be between \$2971.50 and \$4640.07. According to the above values, we can conclude that student pharmacists can have a significant beneficial impact on IV to PO interchange.

Abstract No. 14 (Faculty)

Title

Are Proton Pump Inhibitors Associated with the Development of Community Acquired Pneumonia: A Meta-analysis

Affiliations

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Abstract

Study Objective

To evaluate the association of proton pump inhibitors (PPIs) and community acquired pneumonia (CAP).

Design

Meta-analysis of ten case controlled and cohort studies.

Patients

120,863 pneumonia cases from 1987-2006 were included in the meta-analysis.

Measurements and Main Results

PubMed was searched from inception through May 2011 by two investigators independently using key words: PPI, pneumonia, omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole. This meta-analysis only included case controlled and cohort studies which were published in full in English and evaluated PPI use and CAP incidence. Studies were excluded if they included the following patients: pediatric, H. pylori treatment, and critically ill. Bibliographies of recent review articles and systematic reviews were hand searched. Quality of studies was assessed using the Newcastle Ottawa Quality Assessment Scale (NOQAS). Two investigators independently extracted data into standardized data collection forms which was confirmed by a third investigator. Data were analyzed based on current use of PPIs, duration of PPI use (< 30days, >180days), PPI dose (high versus low), and use of any acid suppressive therapy (Histamine2 Receptor Antagonist or PPI). Overall association of PPI and CAP was analyzed using the random effects model (Comprehensive Meta analysis® Ver 2.0). Nine studies met all criteria for the primary outcome.

NOQAS scores ranged from 4-8 out of 9. Current use of PPIs (OR 1.39, 1.09-1.76), PPI use < 30days (OR 1.65, 1.25-2.19), PPI high dose (OR 1.50, 1.33-1.68) and PPI low dose (OR 1.17, 1.11-1.24) were significantly associated with CAP: There was no association between CAP and PPI use >180days (OR 1.10, 1.00-1.21) or use of any acid suppressive therapy (OR 1.24, 0.99-1.55).

Conclusion

Patients currently receiving PPIs, particularly < 30days or high dose, showed an association with CAP. Practitioners need to be vigilant about adverse effects of PPIs and consider alternative therapies.

Abstract No. 15 (Faculty)

Title

Pulmonary siRNA delivery with biodegradable and biocompatible nanoparticles

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Authors

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Abstract

Purpose:

Pulmonary siRNA delivery mediating direct access to lung epithelium has attracted strong interest and has successfully mediated target gene knockdown in a number of disease models.

Various lipid-based commercially available transfection reagents have been evaluated for pulmonary siRNA delivery as well as the polycation

polyethyleneimine (PEI) and its PEGylated [1] and fatty acid-modified derivatives [2]. However, the gene knockdown mediated by these siRNA formulations was accompanied by remarkably increased cytokine levels in the bronchoalveolar lavage fluid despite reduced cytotoxicity as compared to unmodified PEI [1,2].

Therefore, a biodegradable and biocompatible polymer, poly[vinyl-3-(diethylamino)propylcarbamate-co-vinyl acetate-co-vinyl alcohol]-graft-poly(d,l-lactide-co-glycolide) (DEAPA-PVA-g-PLGA), previously used for pulmonary gene delivery [3] was now adopted for pulmonary siRNA delivery. This polymer was reported not to cause inflammatory responses or recruitment of polymorphic neutrophils into the lung [3], and its siRNA formulation was shown to be suitable for aerosolization [4].

Methods:

Nanoparticles were prepared by solvent-displacement [4], and the formulation at up to 40-fold concentration was optimized as determined by dynamic light scattering and zeta potential measurements. For in vivo experiments, siRNA was radiolabeled as described before [1], and nanoparticles were administered intratracheally to EGFP-expressing mice [1]. Lung retention, systemic availability, and biodistribution were assessed by SPECT imaging, and EGFP knockdown in distinct populations of lung cells was measured according to a newly established flow cytometry-based protocol after differentiating myeloid cells from endothelial cells and type II pneumocytes.

Results:

DEAPA-PVA-g-PLGA nanoparticles of 249 nm and 48 mV were obtained at 40-fold concentration and remained stable in the lung with little systemic availability and 7-fold increased lung retention compared to free siRNA 48 h after pulmonary administration. The strongest EGFP knockdown with 45% was observed in type II pneumocytes 3 days after treatment.

Conclusion:

DEAPA-PVA-g-PLGA nanoparticles are a promising pulmonary siRNA delivery system for knockdown of pathologically overexpressed genes.

References:

- [1] Merkel, O.M., et al., Mol Pharm, 2009. 6(4): 1246-60.
- [2] Beyerle, A., et al., Journal Control Release, 2011. 151(1):51-6

[3] Dailey, L.A., et al., *Toxicol Appl Pharmacol*, 2006. 215(1): 100-8.
[4] Nguyen, J., et al., *J Control Release*, 2008. 132(3): 243-51.

was analyzed using BioEdit sequence analyzing software. PCR and DNA sequencing primers were designed in the lab, and were synthesized by Integrated DNA Technologies.

Abstract No. 16 (Student_Undergraduate)

Title

Preparation of CerS1 & 6 Overexpression Plasmids for Transfection

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Authors

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Janice M. Kranaik
Duska Separovic, Ph.D

Abstract

The cancer treatment modality photodynamic therapy (PDT) can effectively eradicate local malignancies. However, tumor recurrence does occur. To potentiate the efficacy of PDT for cancer treatment, the regulation of pro-death sphingolipids and their role in promoting cell death via apoptosis and autophagy after PDT need to be understood. In the de novo ceramide pathway, ceramide synthase (CerS) catalyzes the reaction in which a fatty acyl component of a new ceramide molecule is added. CerS1 has been implicated in sensitization of cells to anticancer drugs. CerS6 has been associated with apoptosis and autophagy after stress. Our preliminary findings have shown that in CerS6 knockdown cells PDT-induced DEVDase activation is attenuated, suggesting an antiapoptotic role of CerS6. We hypothesize that overexpression of CerS6 and CerS1 will sensitize cells to PDT. The objective of this study was to prepare CerS1 and CerS6 overexpression plasmids for future transfections. The study utilized E. coli culture techniques in order to produce an appropriate amount of plasmid for transfection experiments. The DNA was sequenced by the DNA sequencing Core at Wayne State and

Abstract No. 17 (Faculty)

Title

Analyzing Family Service Needs of Typically Underserved Families in the United States.

Affiliations

Occupational Therapy

Authors

Preethy S. Samuel, PhD, Krim K. Lacey, PhD, Alicia D. Jones, MOT Student

Abstract

Background: Present day service systems evolved from the traditional model of disability intervention where the child with the disability and the family were viewed as pathological entities that needed to be fixed rather than supported. Scholars have increasingly called for a greater focus on the family in service delivery, but few studies have empirically examined the practical reality of such a shift. The present paper examines the disability related formal service supports within the family quality of life (FQoL) framework in a sample of predominantly low-income, minority families in the United States.

Method: Cross-sectional data collected from a convenience sample of 149 families using the FQoLS-2006 was analyzed at the univariate, bivariate and multivariate levels.

Results: Over half of the families indicated that they needed more help from the service system, and the largest barrier to accessing services was a lack of information. Almost all families viewed service support as very important to their overall FQoL, however only half of them were satisfied with the formal support that they were receiving. Less than half of the families reported having many service support opportunities and high attainment of service support, although most took high initiative in

pursuing formal supports. The path model illustrated the complex inter-relationships between the six dimensions of service support.

Conclusions: Findings underscores the need for resources to empower families and the value of using the FQoLS-2006 to ascertain the service support needs and strengths of families.

Abstract No. 18 (Student_Graduate)

Title

PRODRUG DELIVERY VECTORS FOR COMBINATION DRUG/GENE THERAPY: SYNERGISTIC ENHANCEMENT OF TRAIL ACTIVITY IN BREAST CANCER

Affiliations

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Authors

Yu Zhu, graduate student
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David Oupicky, PhD

Abstract

INTRODUCTION

Nonviral gene delivery vectors show promise for cancer gene therapy but they often cause adverse toxic effects and show poor therapeutic response due to low transfection activity. To help address the toxicity and low activity, we propose a new approach to the design of nonviral gene delivery vectors. The traditional design paradigm aims to synthesize biodegradable vectors that are degraded into safe low-molecular-weight byproducts to overcome the adverse toxicity. Here, we propose an alternative approach to this traditional paradigm and design biodegradable vector prodrugs that degrade into active pharmacologic agents. This approach not only reduces toxicity of the vectors but it also enhances activity when combined with properly selected therapeutic gene. The concept of the prodrug delivery vectors is based on polyamine analogues that exploit the self-regulatory nature of the metabolism of cellular polyamines (spermine, spermidine, putrescine). Polyamine metabolism is frequently dysregulated in cancer and other hyperproliferative

diseases, making the polyamine analogues attractive targets for combination drug/gene cancer therapy. N1,N11-bis(ethyl)norspermine (BENSpm) is among the simplest polyamine analogues developed. It induces a polyamine catabolic enzyme, spermidine/spermine N1-acetyltransferase (SSAT), while downregulating ornithine decarboxylase and S-adenosylmethionine decarboxylase, ultimately resulting in cell growth inhibition and apoptosis.

EXPERIMENTAL METHODS

We synthesized asymmetrical lipid analogues of BENSpm with or without biodegradable dithiobenzylcarbamate linker (Lipo-ss-BENSpm and Lipo-BENSpm, respectively). Cell viability in human breast cancer cells was determined by MTS assay (CellTiter 96 □ ... Aqueous One Solution Proliferation Assay, Promega). Combination effect of the BENSpm vectors on TRAIL activity in MDA-MB-231 and MCF7 cells was evaluated by combination index (CI) analysis. Activity of spermidine/spermine N1-acetyltransferase (SSAT) was determined by measuring the radioactivity of [14C]-acetylated spermidine product from the SSAT-catalyzed reaction of [14C]-acetyl-CoA with spermidine. Transfection experiments were performed using gWIZ-luciferase reporter plasmid (Aldevron).

RESULTS AND DISCUSSION

Both synthesized lipid prodrugs mediated transfection comparable to commercial transfection agents. The cytotoxic effects of BENSpm result, in part, from inducing polyamine catabolic enzymes such as SSAT. We found that biodegradable Lipo-ss-BENSpm, which releases free BENSpm after intracellular reduction, induced SSAT to levels comparable to the original BENSpm. The use of LipoBENSpm, however, resulted in the loss of SSAT-inducing activity.

Studies of the combination effect of the BENSpm vectors with TRAIL showed a strong synergistic enhancement of TRAIL anticancer activity in the triple negative breast cancer cells MDA-MB-231. The observed CI values determined by the Chou-Talalay method in MDA-MB-231 were < 0.05 across the entire studied Fa range, indicating a strong synergy between BENSpm and TRAIL. Dose Reduction Index (DRI) denotes how many fold dose reduction is possible for the two agents due to synergism when compared with the dose of each drug alone. The calculated DRIs for BENSpm and TRAIL were 35 and 283, respectively. The finding that ~280-fold lower amount of TRAIL is needed when combined with BENSpm to achieve the same activity

as TRAIL alone suggests substantial benefits of the developed prodrug delivery vectors for breast cancer gene therapy. Strong synergy and suppression of TRAIL resistance was found also in the estrogen-dependent MCF-7 breast cancer cells.

Abstract No. 19 (Faculty)

Title

Neural correlates associated with grasp force matching tasks in older right handed women

Affiliations:

Department of Health Care Sciences, Movement Analysis and Performance Sciences Laboratory, Physical Therapy Program¹; Cognitive Neuroscience of Aging Lab², Wayne State University

Authors:

Rajiv George¹, Ana Daugherty², Diane Adamo¹

Abstract

Introduction:

Central effects on motor behaviors have been significantly advanced by the use of Magnetic Resonance Imaging (MRI) techniques by quantifying functional brain activity, volume and iron concentration of brain structures. Brain structures shrink differentially with age: notable shrinkage in the caudate, putamen and hippocampus; moderate shrinkage in the globus pallidus and entorhinal cortex; and virtually no age-related difference in the primary visual cortex (Raz et al., 2005, 2010). Volumetric differences have been associated with age-related cognitive and motor deficits (Kennedy & Raz, 2005). However, few studies have used structural MRI to investigate changes in sensorimotor control and functions particularly when cognitive demands vary. The purpose of this study was to investigate the neural correlates associated with the perception and reproduction of grasp force in older women in tasks of varying complexity.

Methods:

Seventeen right hand (RH) dominant women (63.5 ± 9.02 yrs; mean laterality index of 0.84 ± 0.18) participated in the study. The influence of hand strength differences on matching performance was also investigated. **Grasp force matching tasks:**

Participants grasped cylindrical devices embedded with strain gauges and performed two matching tasks, based on a 20% maximum voluntary exertion (MVE) reference force. In the Ipsilateral Remembered (IR) condition, the reference and matching forces were produced with the same hand and for the Contralateral Remembered (CR) condition, memorized reference force information was transferred to the opposite hand/hemisphere to produce the match. Two practice trials were followed by three test trials for each hand x condition combination. MRI Scans were performed at the MRI Research Center at Harper Hospital. Dependent variables include: 1) *Relative matching error* – the relative differences between the reference and matching grasp force, 2) *Constant error* – an indication of overshoot and undershoot and, 3) *Correlations* of hand matching performance with MRI data.

Results:

Matching relative error was significantly greater in the CR than IR condition ($P < 0.05$). Directional differences (right hand overshoot, left hand undershoot) in force matching were significant in the CR condition for individuals who showed greater left than right hand strength ($P = 0.05$) and equivalent hand strengths ($P = 0.017$). Directional differences when matching with the opposite hand were significant in the CR condition than IR condition ($P = 0.31$)

Discussion:

The absence of a hand effect in the IR condition shows that the “comparator” of perception is consistent and unbiased. In right handers, the directional error observed in the CR condition indicates an asymmetry between the two systems which may be explained by a difference in gain (higher for the left than right hand/hemisphere). Furthermore, the asymmetry is significant when hand strengths are equivalent and when the left hand is stronger than the right. This interaction suggests that the gain of the motor component plays a significant and primary role. The comparison between the MRI scans and the grip data are currently being processed.

Acknowledgements:

Supported by a Wayne State University Junior Faculty Grant awarded to D.E. Adamo. Zahid Latif, MRI Research Center, for assistance with the MRI data collection.

Abstract No. 20 ()

Title

Test-Retest Reliability of Timed Cervical Flexor and Extensor Endurance Test for Individuals With and Without Neck Pain

Affiliations

Department of Healthcare Sciences, Program in Physical Therapy, Eugene Applebaum College of Pharmacy and Health Sciences

Authors

Rebecca Edwards SPT, Todd Altstetter, SPT, Kyle Weishaupt SPT, Kim Dunleavy Ph.D, PT, OCS

Abstract

Background and purpose: Previous tests have resulted in neck pain or utilize incremental position holds in cervical flexion. The purpose of this study was to determine the intra-rater reliability of modified cervical flexion and extension endurance tests in patients with-and without neck pain. Methods: Twenty four young subjects ... 12 with neck pain and 12 with no neck pain, performed cervical flexion and extension endurance tests (3 trials in two sessions). Recorded time included the time maintained in a neutral isometric cervical position against an inflatable cuff in supine, and time spent against gravity in prone measured with the CROM. Intra-rater reliability was calculated for each researcher using intraclass correlation coefficients (ICC_{3,1}) across 3 trials for each investigator. Within-subject mean flexion and extension times between Sessions A and B across the pain and no pain groups were compared using Repeated Measure Anovas. Pain and Neck Disability functional scores were also compared across times for pre-testing, post-testing, 24 and 48 hours using Repeated Measure Anovas. Results: Isometric flexion endurance in supine was significantly higher in the no pain group ($p < 0.05$) in session A, but there was no difference in Session B. There was a significant difference between sessions A and B for the entire sample ($p < 0.05$), and for the no pain group with longer times recorded in Session A. Extension endurance was not significantly different between the pain and no pain groups, but did decrease significantly from session A to session B in the no pain group and for the entire sample ($p < 0.05$). Overall ICC test-retest reliability for all

examiners for the flexion test was poor (Session A ICC (3,1) single = 0.29 , average = 0.55 , Session B ICC (3,1) single = 0.29, average = 0.55). Extension test-retest reliability was poor in Session A (ICC (3,1) single = 0.13, average = 0.31), but improved slightly in session B (ICC (3,1) single = 0.49, average = 0.74). No significant increases in pain were noted for the pain or no pain groups.a.

Conclusion: The tests as performed in this study showed insufficient intra-rater reliability to be viable tests for measurement of cervical endurance. There was evidence of a learning effect particularly in the no pain group, with overcompensation in the early trials. Some subjects exhibited larger discrepancies for individual trials which may have been related to compensations using the arms or the trunk. The extension endurance test showed higher test-retest reliability in Session B, but requires modifications for future investigations. Possible adjustments for future studies include additional practice sessions, arm positioning to limit use of the arms for the extension test, acceptance of some variation in position prior to stopping timing, and further standardization of instructions. As the tests did not significantly increase pain, refinements of the extension test procedure, as well as additional research standardization with larger number of subjects per investigator are recommended prior to eliminating the tests used in this study as viable alternatives to more aggressive testing.

Abstract No. 21 (Student_Graduate)

Title

A novel, selective inhibitor of bacterial N5-CAIR mutase

Affiliations

Department of Pharmaceutical Sciences
Wayne State University

Authors

Maria V. Fawaz, B.S, Steven M. Firestine, Ph.D.

Abstract

The increasing frequency of drug-resistant bacterial infections has amplified the need for novel antimicrobial agents. De novo purine biosynthesis is

one area that has great potential for antibacterial drug development because this pathway is different in microorganisms versus humans. The difference in the pathway is centered on the synthesis and utilization of the purine intermediate N5-carboxy-5-aminoimidazole ribonucleotide (N5-CAIR). Previous studies have shown that N5-CAIR is a key intermediate in purine biosynthesis in bacteria, yeast and fungi, but not in humans. N5-CAIR is synthesized from 5-amino-imidazole ribonucleotide (AIR) by the enzyme N5-CAIR synthetase (PurK). N5-CAIR is then converted to 4-carboxy-5-aminoimidazole ribonucleotide (CAIR) by the enzyme N5-CAIR mutase. N5-CAIR mutase has been overlooked as an antibacterial drug target due to the structural and sequence relationship with the human enzyme, AIR carboxylase. In an attempt to identify selective inhibitors of N5-CAIR mutase, high-throughput screening (HTS) was conducted using *E. coli* N5-CAIR mutase with a counterscreen against the human AIR carboxylase. These experiments revealed one compound that selectively inhibited *E. coli* N5-CAIR mutase. Additional laboratory analysis confirmed the selectivity profile of this compound. Molecular modeling was performed to better understand the binding mode of the inhibitor against *E. coli* N5-CAIR mutase and human AIR carboxylase. In this poster, we will present the results of the HTS, the enzymatic characterization of the inhibitor and our molecular modeling results to determine the reason for the selectivity observed in the compound.

Abstract No. 22 (Student_Graduate)

Title

The Effect of Extended Head Position on Postural Sway In Young Adults

Affiliations

Department of Healthcare Sciences, Program in Physical Therapy and Institute of Gerontology, Wayne State University, Detroit, Michigan, 48201.

Authors

Nora Palanjian, SPT, Farah Khan, SPT, Mariam Naqvi, SPT, Fredrick D. Pociask, PT, PhD, Allon Goldberg, PT, PhD

Abstract

INTRODUCTION: Postural control is defined as the ability to maintain equilibrium in a gravitational field by maintaining the center of body mass over its base of support. The purpose of our study was to examine the changes in postural sway caused by alteration of vision, foot somatosensation and vestibular orientation in young healthy adults. We hypothesized that the extended head position with the absence of vision and distorted foot somatosensation would increase postural sway. **METHODS:** Sixty healthy male and female students (mean age = 24.2 years, male = 22, female = 38, and range = 21-31 years) completed a questionnaire and postural sway testing using a force plate. The questionnaire included biographical data, a basic neurological and ENT review of systems, and screening for current and/or previous medical and surgical history. Postural sway testing was conducted using two surfaces (firm and foam), two visual conditions (eyes open and closed), and two cervical conditions (head neutral and extended) for a total of eight measures. A cervical range of motion (CROM) device was used with all conditions to ensure the head was held in neutral or extended positions. A 2 surface (firm and foam) x 2 head position (neutral and 45 degrees) x 2 visual (eyes open and closed) repeated measure ANOVA was used to evaluate main effects of surface, vision and head position, as well as interactions among these conditions, on postural sway. Significance was set at $p < 0.05$. **RESULTS:** A main effect of surface: partial eta squared = 0.96, foam (1.26 degrees/second) > firm (0.33 degrees/second), $p < 0.001$... a main effect of vision: partial eta squared = 0.93, eyes closed (1.11 degrees/second) > eyes open (0.48), $p < 0.001$, and a main effect of head position: partial eta squared = 0.52, extension (0.85 degrees/second) > neutral (0.74 degrees/second), $p < 0.001$ were detected. A significant three-way interaction effect (partial eta squared = .61, ($p < 0.001$) was detected: when standing on a foam surface with eyes open or eyes closed, head position had an effect on postural sway, ($p < 0.01$). However when standing on a firm surface with eyes open or closed, head position had no effect on sway ($p > 0.05$). Pairwise comparisons indicated that the greatest amount of sway was observed when standing on foam with eyes closed and the head extended (2.07 degrees/second), followed by standing on foam with eyes closed and the head in neutral position (1.59 degrees/second) ($p < 0.001$). **DISCUSSION AND CONCLUSION:** Our hypothesis that the extended head position with the absence of vision and distorted foot somatosensation would increase postural sway, is supported by these results. Results from this study

contribute to the understanding of the effects of vision, surface condition and head position, as well as the interaction between these three variables on postural sway in young healthy adults. Future studies will seek to better understand how balance may be impacted in young adults with impairments impacting vestibular and foot somatosensory function. This study should also be replicated in older adults with balance impairments.

Abstract No. 23 (Student_Graduate)

Title

Pulmonary absorption and organ distribution of polystyrene nanoparticles

Affiliations

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Authors

Abdul Khader Mohammad, B.Pharm(Hons.), Joshua Reineke, PhD

Abstract

The lungs possess many advantages as an administration pathway including an alveolar surface area of around 100m², high solute permeability, limited proteolytic activity, a very thin alveolar epithelium of 0.2µm, and extensive vasculature. The understanding of nanoparticle uptake and biodistribution from lungs in relation to their physicochemical properties from a drug delivery perspective is limited. It has been reported that nanoparticles translocate to the lymph nodes from lungs. Therefore, we studied the effect of nanoparticle size on their uptake and biodistribution in general and on their lymph node deposition in particular. Different nanoparticle sizes were selected based on the fact that the nanoparticle uptake mechanisms vary with size. Most studies investigating biodistribution of polymer nanoparticles use a fluorescent probe as a way to track nanoparticles in vivo. Here, by using the gel permeation chromatography (GPC) based detection technique we quantitatively determine the pulmonary uptake potential and biodistribution of PN without the use of fluorescent markers.

At 1 hour post administration of PN, the total uptake was lowest for the smallest size PN and increased with size. However, at 3 and 5 hour time points, the total uptake was highest for the smallest size and it decreased with an increase in size. Furthermore, the most interesting finding from this research was that a major proportion of the absorbed PN distribute to lymph nodes from lungs and in small amounts to other tissues. This observation holds true for all the sizes of PN studied though the extent of lymph node deposition varies from one size to other. Additional studies performed by administering the particles via intratracheal instillation showed no statistically significant differences in the uptake and biodistribution of PN as compared to those administered by pharyngeal aspiration. Similar biodistribution studies were performed by washing the PN in distilled water and reconstituting them in normal saline to confirm that the results obtained are not as a result of the suspension media. However, the washed nanoparticles had no statistically significant results as compared to the PN used as purchased. These tests further confirm the absorptive potential of lungs for nanoparticles and their preferred deposition in lymph nodes.

The specificity of PN for lymph nodes over major organs, especially over organs of the reticuloendothelial system that play an active role in clearing polymer nanoparticles from the blood is a remarkable result. When expressed as µg/g of tissue, the lymph nodes have a deposition range of 1000-3500µg/g of tissue. The highest deposition is for the 50nm size (3497 µg/g of tissue) and lowest for the 900nm size (1044 µg/g of tissue). Considering the small size and weight of the lymph nodes, this is a significant amount of deposition and may indicate localized therapeutic potential. Therefore, the significant amount of uptake from lungs in the short time period of 5 hours in addition to the high propensity of PN distribution to the lymph nodes uncovers the potential of nanoparticulate pulmonary drug delivery systems for systemic use in general and for lymph-targeted therapies in particular.

Abstract No. 24 (Student_Graduate)

Title

Novel, multifunctional drug D-264 for Parkinson's disease: Evidence of neuroprotective property in MPTP and lactacystin PD animal models.

Affiliations

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Authors

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Abstract

Parkinson's disease (PD), a progressive neurodegenerative movement disorder, is known to be caused by diverse pathological conditions. Dysfunction of the ubiquitin-proteasome system (UPS), mitochondria, and oxidative stress lead to preferential, nigral dopamine (DA) neuron degeneration in the substantia nigra. To slow the neurodegeneration in PD, several pathological pathways leading to this disease should be intervened. In the present study, we found that D-264 significantly improved behavioral performances and attenuated significantly: MPTP and lactacystin induced DA neuron loss, proteasomal inhibition, and microglial activation in substantia nigra (SN). Furthermore, D-264 treatment was shown to increase levels of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF) in MPTP and lactacystin treated mice, partially indicating a mechanism of neuroprotection by D-264. Our study indicates that multifunctional drug, D-264, can attenuate neurodegeneration induced by the selective neurotoxin, MPTP and UPS inhibitor, lactacystin and may serve as an improved and better neuroprotective treatment agent for PD.

Abstract No. 25 (Student_Graduate)

Title

Discovery of multifunctional molecules possessing dopamine agonist activity at D2/D3 receptors along with iron chelation and antioxidant activities: Pharmacological characterization in vitro and in vivo

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Authors

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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 our overall goal to develop bifunctional/multifunctional drugs as neuroprotective treatment agents for PD, we designed dopamine D2/D3 agonist molecules with the 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 with GTPγ ... S binding assay. SAR results identified compounds with potent agonists activity at both D2 and D3 receptors (EC₅₀ (GTPγ ... S) ... D2 = 4.51, 1.69, 34.0 nm and D3 = 1.58, 0.74, 6.83 nM,

respectively). In vitro complexation studies of (-)-D-369 and (-)-D-390 demonstrated efficient chelation with iron by both UV visible and mass spectroscopy methods. Furthermore, the deoxyribose and DPPH assays with the lead molecules (-)-D-369 and (-)-D-390 demonstrated potent antioxidant activity. In PD animal model studies, lead molecules (-)-D-369 and (-)-D-390 exhibited efficacious in vivo activity in reversing locomotor activity in reserpinized rats and also in producing potent rotational activity in 6-OHDA lesioned rats. In cell culture study, the selected compounds demonstrated significant reduction of toxicity induced by treatment with either Fe²⁺ and MPP⁺, thereby, producing neuroprotection effect.

Abstract No. 26 (Student_Graduate)

Title

MESOPOROUS SILICA NANOPARTICLES FOR DELIVERY OF HYDROPHILIC-HYDROPHOBIC DRUG COMBINATIONS

Affiliations

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Authors

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Abstract

INTRODUCTION

Combinations of two or more chemotherapeutic agents with synergistic or additive effects have been used effectively in cancer therapy protocols. Mesoporous silica nanoparticles (MSN) emerged as a promising platform for delivering drug combinations. The main advantage of MSN over other delivery platforms is their ability to encapsulate drugs with a broad range of physicochemical properties (hydrophobic, hydrophilic), something that other delivery vectors, such as micelles or polyester nanoparticles, are not typically capable of. The goal of this study was to evaluate the suitability of MSN to deliver combination of hydrophilic and

hydrophobic anticancer drugs.

EXPERIMENTAL METHODS

Thiol-, amine-, and mixed thiol/amine-functionalized MSN were synthesized and characterized by electron microscopy, thermogravimetry, and surface area analysis. The surface functional groups were determined by elemental analysis and zeta potential measurement. Drug loading was determined by UV-Vis spectroscopy and thermogravimetry. Effect of surface functional groups on drug release kinetic was determined in phosphate buffered saline (pH 7.4) and in 0.15 M sodium acetate (pH 4.5). Fluorescence quenching of mitoxantrone (MTX) after encapsulation was confirmed by fluorometer. Crystalline/amorphous state of drugs encapsulated in MSN was determined by differential scanning calorimetry and powder X-ray diffraction.

RESULTS

The loading of hydrophilic drug MTX was found to depend strongly on the type of surface functional group modification of MSN. Thiol-modified MSN showed high MTX loading when compared to thiol/amine and amine-modified MSN. MTX loading resulted in an increased zeta potential of MSN. MTX release was strongly dependent on the pH of release medium and the nature of surface functionalization of MSN. Curcumin (CRM) was investigated as an example of a hydrophobic drug. The total loading of the CRM and MTX drug combination was 210 mg/g MSN. Both CRM and MTX were found in their amorphous forms when loaded in the MSN. No significant effect of CRM presence on MTX release was observed.

CONCLUSION

Inorganic material like MSN offer an interesting alternative to organic formulations such as polymeric nanoparticles, micelles and liposomes due to excellent drug loading capacity, high surface area, compatibility with wide range of drugs and non-toxic degradation products. We demonstrated how optimization of MSN surface properties improves drug loading and control of the release kinetics. We successfully achieved loading and release of hydrophilic/hydrophobic drug combination, thus demonstrating the potential of MSN for delivery of drug combinations.

Abstract No. 27 (Faculty)

Title

Novel triple dopamine, serotonin and norepinephrine transporters blockers as potent antidepressant: Characterization of a lead molecule in in vitro and in vivo pharmacological assays

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Authors

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Abstract

Major depression disorder is a significant health problem and about 10-20% of all adult population suffers from this disease. Unipolar depression is ranked as number one before all other somatic and psychiatric illnesses. In spite of its prevalence, the underlying causes of depression are still unclear and 15% of depressed patients are resistant to all known therapies. Monoamine therapies have so far been most successful and have been used most widely to treat depression. Triple monoamine reuptake inhibitors have recently been implicated in generation of potent antidepressant activity with possible lowering of side effects profile. The underlying involvement of dopaminergic system in depression prompted our efforts to develop triple reuptake inhibitors, which are expected to produce strong antidepressant effects in addition to the treatment of anhedonia. For this purpose, we have recently demonstrated the development and synthesis of novel asymmetric trisubstituted and disubstituted pyran derivatives as inhibitors of monoamine transporter systems in the CNS. Number of other molecules from this series also displayed triple reuptake inhibitory activity. Molecules with triple uptake blocking activity exhibited low nano-molar affinity at the norepinephrine transporter followed by potent to good affinities at the both serotonin and dopamine transporters. One of the lead selected compounds, D-142, exhibited uptake inhibition (ki) values of 29.3

nM, 14.7 nM and 37.4 nM for the norepinephrine, serotonin and dopamine transporters, respectively. This compound was next tested in two well established in vivo animal models for antidepressant activity. Thus, in vivo rat forced swimming test and mouse tail suspension test were carried out to evaluate potential of this compound as an antidepressant agent. In rat forced swimming test, compound D-142 exhibited potent antidepressant activity in the dose range tested and was far more potent than the reference Imipramine. In mice tail suspension test, compound D-142 exhibited potent effect in reducing immobility in a dose dependent manner, indicating potent antidepressant effect. In locomotor activity test, compound D-142 did not exhibit any locomotor stimulation in the dose range tested. In the extended CNS receptors screening assay this molecule exhibited no non-specific interaction in the CNS. These results indicate that D-142 might possess potent antidepressant activity.

Abstract No. 28 (Student_Graduate)

Title

Shell-Cleavable PLGA-Curcumin Conjugate Micelles

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Authors

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(First,Last):Joshua Reineke Degree: PhD.

Abstract

Curcumin (diferuloylmethane) is a derivative of the herb of *Curcuma longa*, which has multiple applications in the treatment of many diseases as well as having anticancer effect.

Unfortunately, curcumin has low oral bioavailability

and its tissue distribution is very limited. To overcome the bioavailability problem, protection of it from metabolic system is greatly preferred and many approaches have been pursued.

Water-soluble formulation of curcumin was reported by conjugation of curcumin with polyethylene glycol (PEG), which showed a greater inhibitory effect on the proliferation of a pancreatic cell line compared with free curcumin. The curcumin-PEG conjugate can be used to fabricate nanoparticles or micelles for protection and delivery of curcumin so to provide better pharmacokinetics properties than simply encapsulated curcumin.

PLGA or poly(lactic-co-glycolic acid) is a copolymer which is approved by the FDA for applications in therapeutic devices due to its biocompatibility and biodegradability was used to conjugate curcumin onto biocompatible polymer to increase its bioavailability and to explore the anticancer effect of this drug. We demonstrated removable shell micelles based on PEG-SS-PLGA-curcumin. The molecular structure of the PEG-SS-PLGA-curcumin conjugate was confirmed by ¹H NMR, FTIR and GPC. Free curcumin was released from the micelles in a reductive solution mimicking the intracellular environment. However, in PBS buffer free of reducing agents the micelles were stable and released little curcumin. Thus, we envision the reductive-responsive micelles to be used for an extended circulation time, protection from rapid clearance and, finally, the cytoplasmic delivery of curcumin.

Abstract No. 29 (Post_Doctoral_Fellow)

Title

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

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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. 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 critical role in substrate binding and catalytic activity of enzyme, as identified from crystallographic and computational studies. These residues were mutated to alanine, glutamine, lysine, arginine and phenylalanine ... the resulting mutated enzymes were analyzed by steady-state kinetics and equilibrium dialysis. The results of these studies will be presented.

Acknowledgements: Financial support for this work was provided by NIH (R01GM087467).

Abstract No. 30 (Student_Graduate)

Title

Indomethacin Inhibits Microglial Activation: Evidence from In vitro and In vivo Experimental Studies

Affiliations

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Authors

Abiy M. Mohammed, Mrudangkumar M. Shah and David M. Thomas

Abstract

Microglia play a critical role in maintaining a healthy environment in the central nervous system. However, when activated, they release inflammatory mediators which can be injurious to healthy cells. Results have shown that damage to dopaminergic nerve terminals following exposure to neurotoxic amphetamines (like methamphetamine) is associated with microglial activation. The objectives of this study were to examine the neuroprotective properties of indomethacin using in vitro and in vivo models. BV-2 cells, an immortalized microglia cell line, were exposed to lipopolysaccharide (LPS) from *Escherichia coli* for one hour in the absence or presence of different concentrations of indomethacin, and the levels of inflammatory mediators such as COX-2 expression and TNF-alpha secretion were measured. For the in vivo studies, mice were exposed to a single dose of methamphetamine and the neuroprotective effects of indomethacin on dopamine depletion, GFAP activation, DAT expression and ILB4 staining were examined. In both models, indomethacin inhibited inflammation and microglial activation. These results suggest that indomethacin may prevent the dopaminergic nerve terminal damage that is associated with microglial activation following neurotoxic methamphetamine exposure.

Abstract No. 31 (Student_Graduate)

Title

Effects of Wii Fit on Balance Impairments in Post-stroke Rehabilitation

Affiliations

Wayne State University

Authors

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Abstract

Background and Purpose: Stroke can result in significant changes in balance that can cause increased risk of falls. Research has shown the Wii Fit is an optimal tool in improving overall strength and balance, but little evidence has shown the effectiveness of the Wii Fit on balance impairments in post-stroke rehabilitation.

Participants: Participants were 3 men and 1 woman with a history of one chronic stroke, who could stand for 20 minutes with or without an assistive device.

Intervention: Participants trained 2 times a week, on non consecutive days, for 6 weeks using the Wii Fit Balance Board and table tilt game. Target training was 20 minutes with rest breaks taken as needed.

Outcomes: Outcome measures were assessed within 1 week before and after training, and included the Activities-specific Balance Confidence (ABC) scale and the BalanceMaster. All participants showed improvements in the ABC scale and BalanceMaster scores.

Discussion: The Wii Fit appears to be feasible and easy to use for individuals at home or in a rehabilitation setting. Positive changes seen with training may lead to improvements in balance and may lead to improvements in functional mobility.

Abstract No. 32 (Post_Doctoral_Fellow)

Title

PBPK-modelling and property biodistribution relationship of PLGA-mPEG nanoparticles

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Authors

Mingguang Li, PhD, Joshua Reineke, PhD

Abstract

Biodistribution of nanoparticles is dependent on their physicochemical properties (such as size, surface charge, and surface hydrophilicity). Clear and systematic understanding of nanoparticle properties' effects on their in vivo performance is of fundamental significance in nanoparticle design, development and optimization for medical applications and toxicity evaluation. In the present study, a physiologically-based pharmacokinetic (PBPK) model was utilized to interpret the effects of nanoparticle properties on previously published biodistribution data. Biodistribution data for five poly(lactic-co-glycolic) acid (PLGA) nanoparticle formulations prepared with varied content of Monomethoxypoly (ethyleneglycol) (mPEG) (PLGA, PLGA-mPEG256, PLGA-mPEG153, PLGA-mPEG51, PLGA-mPEG34) were collected in mice after intravenous injection. A PBPK model was developed and evaluated to simulate the mass-time profiles of nanoparticle distribution in tissues. In anticipation that the biodistribution of new nanoparticle formulations could be predicted from the PBPK model, multivariate regression analysis was performed to build the relationship between nanoparticle properties (size, zeta potential, and number of PEG molecules per unit surface area) and biodistribution parameters. Based on these relationships, characterized physicochemical properties of PLGA-mPEG495 nanoparticles (a sixth formulation) were used to calculate (predict) biodistribution profiles. For all five initial formulations, the developed model adequately simulates the experimental data indicating that the model is suitable for description of PLGA-mPEG nanoparticle biodistribution. Further, the predicted

biodistribution profiles of PLGA-mPEG495 were close to experimental data, reflecting properly developed property-biodistribution relationships.

Abstract No. 33 (Student_Graduate)

Title

Physical and Functional Fitness in Older Adults

Affiliations

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- Movement Analysis and Performance Sciences Laboratory (MAPS), Wayne State University
- Oakwood Common Independent and Retirement Living Community

Authors

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Abstract

Introduction: Physical activity is an important marker for assessing the quality of life with aging. Participating in physical activity contributes to improvements in general health and thinking abilities and, reduces the risk of chronic diseases. Declines in physical activity may contribute to reductions in cognitive abilities, muscle strength, aerobic endurance, flexibility and balance that, in turn, may lead to difficulties when caring for one's self independently. The purpose of this study was to investigate the relationship between functional fitness, self reported physical activity and cognitive abilities in a group of older adults.

Methods: Fourteen healthy, older adults from Oakwood Common Independent and Retirement Living Community participated in the study. Participants were required to walk independently and score 24 on the Mini Mental State Exam (MMSE) to partake in the study. Cognitive assessments included the Trail Making Tests (TMT) parts A and B. The Senior Fitness Test (SFT) assessed upper and lower

body strength, flexibility, dynamic balance and aerobic endurance. Self-reported physical activity was obtained from the Community Health Activities Model Program for Seniors (CHAMPS).

Results: SFT measures were determined for each participant and compared against standardized norms. When grouped according to gender, men completed more arm curl repetitions than women ($p = 0.04$). Overall, women more than men, scored below threshold values and were placed in the “at risk for loss of functional mobility” category. For the CHAMPS, leisure walking was the most frequently reported activity. However, only general conditioning and the two-minute step test were correlated ($p = 0.026$, $r = 0.593$) showing that higher energy expenditures were related to a greater number of steps taken. Slower TMT-A scores were related to fewer steps taken in the two-minute step test ($p = 0.003$, $r = -0.73$). However, for TMT-B and steps taken, only a trend was found, most likely due to greater variability of TMT-B scores.

Discussion: Findings showed that women were identified as having greater aerobic endurance deficits, while men were identified as having greater deficits in flexibility. It is suggested that optimizing exercise programs specific to the needs of the individual rather than a more generalized approach will contribute to better overall fitness and reduce the risk of loss of functional mobility. Although functional fitness was related to some aspects of cognition and self-reported physical activity, the small sample size restricted an investigation of these factors to overall functional fitness. Moreover, this study was reflective of an “older” population who are not living independently in their own home, but needing the support of a living environment. Generally, this population is largely ignored in studies investigating healthy older populations.

Abstract No. 34 (Student_Undergrad)

Title

Factors associated with 30 day readmission in Staphylococcus aureus bacteremia (SAB)

Affiliations

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Authors

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Abstract

Background : Hospital readmissions are a serious concern in pts with infectious diseases. SAB is a common infection for which quality indicators (QI) are suggested in the IDSA guidelines. It is unknown whether these QI have a beneficial impact on resource utilization, such as hospital readmission. Methods : Retrospective cohort study examining pts, over the age of 18, with SAB between 12/31/09 and 5/31/10. Data was analyzed to identify characteristics associated with all cause 30 day readmission. Results: 57 pts with SAB were evaluated, median time to adequate therapy was 7 hours. The most common sites of concomitant infection were: bone/joint 25%, skin/soft tissue 21%, and respiratory 16%. In hospital mortality was 9/57 (16%), leaving 48 pts evaluable for readmission. Of these, 28 (58%) were readmitted. Pt characteristics are summarized in table 1. In multivariate regression, adjusting for age and ID consultation, only inadequate duration of therapy (< 14 days) remained predictive of readmission. Notably, pts seen by ID consult were older, more often infected with MRSA, and more likely to have endocarditis, bone/joint, or device-related infections. These pts were also more likely to receive an adequate duration of therapy. Conclusion : Over half of pts with SAB are readmitted to the hospital within 30 days, regardless of compliance with guideline recommendations. Other modifiable factors, such as transition of care planning, should be evaluated in future studies.

Abstract No. 35 (Student_Graduate)

Title

Minimal Detectable Change in Maximum Step Length, Gait Speed, and Five Times Sit to Stand in People with Stroke

Affiliations

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Authors

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1)Department of Healthcare Sciences, Program in Physical Therapy, Mobility Research Laboratory, and 2)Institute of Gerontology, Wayne State University

Abstract

Purpose/Hypothesis: The Maximal Step Length Test (MSL) is a test of stepping capabilities and clinical balance in older adults. Gait speed (GS) and the Five Times Sit to Stand (FTSTS) test (time needed to sit and stand five times) are measures of functional mobility. 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 MSL, GS and FTSTS in people who have had a stroke.

Number of Subjects: Twenty participants with a history of chronic stroke who could walk without physical assistance were recruited from the Metro Detroit area.

Materials/Methods: MSL was assessed by having the participant step forward maximally and return in one step. Gait speed was measured as the time it took to walk 10 meters at a comfortable pace (expressed as m/sec). FTSTS was recorded as the time it took to sit and stand five times with arms crossed. 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 $\times \sqrt{1-ICC}$. MDC at a 95% confidence level (MDC95) was calculated as

$z \times SEM \times \sqrt{1-ICC}$ where $z=1.96$.

Results: Mean FTSTS was 19.0 seconds, with an ICC of 0.92 (SEM was 3.28sec, MDC95 was 9.09 sec). Measurement error and MDC95 expressed as a percentage of mean FTSTS were 17.3% and 47.8% respectively. Mean GS was 0.73m/s, with an ICC of 0.98 (SEM was 0.04m/s, MDC95 was 0.11m/s). Measurement error and MDC95 expressed as a percentage of mean GS were 5.5% and 15.1% respectively. Mean MSL (involved) was 20.86", with an ICC of 0.98 (SEM was 1.1", MDC95 was 3.05"). Measurement error and MDC95 expressed as a percentage of mean MSL (involved) were 5.2% and 14.5% respectively. Mean MSL (uninvolved) was 21.5", with an ICC of 0.98 (SEM was 1.39", MDC95 was 3.85"). Measurement error and MDC95 expressed as a percentage of mean MSL (uninvolved) were 6.5% and 17.9% respectively.

Conclusions: The high ICC for FTSTS, GS and MSL suggest high test-retest reliability. FTSTS has a very high MDC% (47.8%) and therefore low sensitivity to detecting real change. GS and MSL (involved and uninvolved) have much lower MDC% and greater sensitivity to detect real change in performance. The low SEM% for GS, MSL (involved) and MSL (uninvolved) is suggestive of low measurement error and good absolute reliability, whereas the opposite is true for the FTSTS.

Clinical Relevance: In patients with chronic stroke, real change was computed to be >0.11 m/s for GS, >3.05 " for MSL (involved), >3.85 " for MSL (uninvolved), and >9.09 sec for FTSTS. These results will assist clinicians and researchers in interpreting whether real change has occurred when comparing repeated measures of FTSTS, GS and MSL.

Abstract No. 36 (Student_Graduate)

Title

Correlation of Calcaneal Bone Stiffness and Plantar Flexor Muscle Strength and Endurance in Elite Runners: A Cross-sectional Analysis

Affiliations

Department of Healthcare Sciences, Program in Physical Therapy, Human Performance Laboratory

Authors

Sean Ellis, BS SPT Derek Bustos, BS SPT Jordan Ball, BS SPT Dr. Thomas Birk PhD, MPT

Abstract

Study Design: Controlled cross-sectional analysis
Background: Repetitive trauma lower extremity injuries are a common occurrence among all levels of athletes, from the “Weekend Warrior” to the professional level. Yet the best means of addressing this particular issue prophylactically have yet to be identified in current rehabilitation literature. Although several studies have attempted to address this issue from a muscular perspective, most have yet to correlate such pertinent results with such critical bone mineral characteristics as density and stiffness. Objective: The purpose of this research endeavor is to explore the existence of potential relationships between plantar muscle strength and endurance with calcaneal bone mineral stiffness across groups of different genders and activity levels. Methods: Males and females ranging in age from 18-25 years of age were recruited from the campus of Wayne State University (n=30) and placed into the experimental group (regular training regimen for distance running, >50 miles/week) or control group (no physical activity >15 minutes after warm-up for >3 days/week). Each subject’s dominant leg calcaneal bone mineral stiffness, plantar flexor muscle strength and endurance was tested and recorded using various standardized and sensitive protocols. Specifically, bone mineral stiffness was measured using the GE Achilles Express and both plantar flexor muscle strength and endurance were assessed using the BIODEX measurement device and a repeated standing heel raise test, respectively. Results: Upon statistical analysis, no significant differences in calcaneal bone mineral stiffness (p = .243) or the heel raise test were noted when

controlled for gender (p=.985). The collected data also produced no significant relationships between body mass index and calcaneal bone mineral stiffness (R= -0.89), nor between bone mineral stiffness and peak plantar flexor torque (R=.183). However, a statistically significant (p= .028) fair positive correlation (R = .401) was indeed determined to exist between bone mineral stiffness and the heel raise test. Further analysis also determined that the running group demonstrated statistically significant increases in both bone mineral stiffness (p = .001) and the heel raise test (p=.001) relative to the control group. Despite this, no statistically significant difference existed between the groups in relation to maximum plantar flexor torque (p=.430). Conclusion: A fair positive correlation was determined to exist between calcaneal bone mineral stiffness and plantar flexor muscle endurance, and thus, potentially suggests to the evidence-based rehabilitation practitioner that muscular endurance training may be more beneficial in reducing the likelihood of future repetitive osseous trauma injuries in the young adult running athlete. Key Words: running, bone mineral density, heel raise, plantar flexor torque

Abstract No. 37 (Student_Graduate)

Title

Comparison of Ground Reaction Force Impact on Medicare Prescribed K3 and K4 Prosthesis During Community Ambulation

Affiliations

WSU

Authors

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Abstract

INTRODUCTION: The Medicare Functional Classification Levels (MFCL) are used to establish the functional level of lower limb amputees, known as K-level. The K-level is determined by an amputee’s projected functional ability early in the patient’s rehab. Differences exist in the prosthetic component’s that are reimbursed by third party payers

based on K-level assignment. The MFCL states that both K-3 and K-4 levels are able to display a variable cadence that can be adapted based on the external environment. However, K-4 patients “[have] the potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress.” Currently the level of force distribution in certain ambulatory activities between the K-3 and K-4 levels is still unknown. These differences in K-3 and K-4 levels may limit the prosthetist’s ability to provide the most adequate prosthetic components that match with an individual’s functional abilities. The purpose of this research is to evaluate the force placed on the prosthesis during functional ambulatory activities in individuals classified as K-3 and K-4 level lower-limb amputees to evaluate if daily ambulatory barriers (steps, curbs, ramps) place a significantly higher stress/force on amputee.

METHODS: A total of 6 participants of K3 and K4 levels were recruited from Wright and Filippis Co. Participants were required to meet the following criteria: 18 years or older, 1yr post-transfemoral amputation, functional assessment at K-3 or K-4 level, use of transfemoral prosthetic limb >5 days/week, and 1 year post transfemoral amputation. A within subjects design was utilized. The Compas™ force collection device was placed on prosthesis by a certified prosthetist to determine quality & quantity of GRF. Participants completed the general information and mobility portion of the PEQ (Prosthesis Evaluation Questionnaire). Circumference of the mid thigh (muscle belly), height, & weight were also taken for each participant.

RESULTS: Paired sample t-tests revealed significant differences between level ambulation and *barrier ambulation (*barrier ambulation includes ambulating over ramps, curbs, and/or stairs). No significant difference was observed between gait velocity and force quantity between the SACH and DYNAMIC foot with all types of ambulation surfaces (barriers and none). A trend displaying increased amounts of force was noted under the descriptive statistics gathered between the levels vs. community barrier ambulation.

DISCUSSION AND CONCLUSION: The force on the prosthesis was significantly higher than comfortable walking force during stair descent, stepping of a big/small curb and ambulating up an incline. The preliminary results indicate further research needs to be performed to evaluate the level of force required for daily ambulatory barriers with the prosthetic individual. Based on these finding it is reasonable to consider these barriers could require more force for the amputee patient and the level of

force could be considered “high impact, stress”. This would bring many K-3 amputees to a K-4 level. Further studies to evaluate ambulator forces differences between individuals described as K-3 or K-4 ambulators needs to continue. Additional subjects should be added in order to determine the significant difference of force placed on the prosthesis between individuals classified as K-3 and K-4 ambulators.

Abstract No. 38 (Faculty)

Title

Overexpression of parkin in rat nigrostriatal system protects against methamphetamine neurotoxicity

Affiliations

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Authors

Anna Moszczynska, Ph.D., Assistant Professor and Bryan K. Yamamoto, Ph.D., Professor and Chair

Abstract

Methamphetamine (METH) is a highly abused psychostimulant drug that, when administered at high doses to experimental animals, causes a selective degeneration of dopaminergic (DAergic) terminals in the striatum. Parkin is an ubiquitin E3 ligase able to protect neurons from diverse cellular insults, suggesting a central role for parkin in maintaining DA neuron integrity. We have previously shown that METH decreases parkin levels in rat striatum. The present study has examined whether upregulation of parkin protects against METH neurotoxicity. Sprague-Dawley rats overexpressing parkin in the striatum were generated by stereotaxic injection of parkin-containing AAV2/6 transfer vector into the left substantia nigra. Striatal tissue was examined for the levels of parkin and two DAergic markers, DA transporter (DAT) and tyrosine hydroxylase (TH) 21 days after microinjections. Striata from hemispheres injected with AAV2/6-parkin showed higher parkin levels than striata from non-injected hemispheres. The levels of DAT and TH were not different

between hemispheres, suggesting that overexpression of parkin does not affect DAergic system in rats. Subsequently, wild type and parkin-overexpressing rats were treated with METH (10 mg/kg, every 2 h x 4, i.p.) or saline (1 ml/kg) and perfused with 4% paraformaldehyde 7 days later. The brains were frozen and examined for METH toxicity to DAergic terminals by measuring TH immunoreactivity in the striatum. In METH-treated parkin-overexpressing rats, TH immunoreactivity decreased to a lesser degree in AAV2/6-parkin-injected hemispheres than in non-injected hemispheres. The results suggest that overexpression of parkin can protect DAergic terminals, whereas decreases in parkin function might contribute to METH neurotoxicity. This work was supported by NIH grants DA023085 and DA07606

Abstract No. 39 (Faculty)

Title

The "CRE score": a bedside score to shorten the time to initiation of effective therapy for carbapenem-resistant Enterobacteriaceae

Affiliations

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Authors

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Abstract

Background: Patients infected with carbapenem-resistant Enterobacteriaceae (CRE) often require polymyxin therapy which is toxic. There is often delay in initiation of appropriate antimicrobial therapy (DAAT). A bedside score was developed to differentiate bloodstream infections (BSI) caused by CRE from BSI caused by ESBL, in order to reduce DAAT and mortality rates associated with BSI.

Methods: Data for patients with CRE and ESBL BSIs from DMC from 2007-2010 were abstracted from charts. A multivariate model for presence of CRE was generated using stepwise methods, with additional inclusion of a priori identified CRE risk factors. A clinical prediction score was derived.

Results: 166 patients with ESBL BSIs and 16 patients with CRE BSIs were included. The prediction score included history of neurologic disease (14 points), diabetes mellitus (12 points), ICU stay at time of infection (11 points), dependent functional status upon admission (7 points), and history of recent (3 months) antibiotic use (7 points). The CRE score had an area under ROC curve of 0.81 (CI-95% 0.68-0.92). A score of \geq ... 32 to define "high CRE risk" had sensitivity of 81%, specificity of 70%, PPV of 20% and NPV of 97%.

Conclusions: The CRE Score is a simple bedside algorithm that can assist in early identification and treatment of patients at risk for CRE BSI. The score's high NPV might help to limit empiric overuse of polymyxins.

Abstract No. 40 (Faculty)

Title

Epidemiology of Respiratory Viral Coinfections in Daycare Attendees

Affiliations

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University of Washington, Seattle Children's Research Institute, Seattle, WA

Authors

Emily Martin, MPH PhD
Mary Fairchok, MD
Jane Kuypers, PhD
Janet Englund, MD

Abstract

Background: The epidemiology and impact of respiratory viral coinfection is not well-known, particularly in mild illness not requiring medical care.

The identification of viral coinfections is increasing as more respiratory viruses are identified and multiplex viral testing becomes more available.

Methods: 225 daycare attendees (ages 1-24 mo.) in Fort Lewis, WA were prospectively followed for up to 2 years. Nasal swabs were collected at respiratory illness onset and every 7-10 days until illness resolution and tested by PCR for human metapneumovirus, respiratory syncytial virus (RSV), parainfluenza types 1-4, influenza A and B, rhinoviruses (RhV), coronaviruses, human bocavirus-1, and adenoviruses (AdV).

Results: 466 new-onset illnesses were captured. At least 1 respiratory virus was detected in 384 (82%) illnesses with multiple viruses identified in 212 (45%). Up to 5 viruses were identified during single illnesses. Specific coinfection rates ranged from 66% in RhV illnesses to 87% in AdV illnesses. The detection of specific viruses at the time of the onset of illness symptoms varied, leading to differences in prevalence of individual viruses based on time since illness onset. For example, 52 of 53 (98%) RSV detections occurred at the beginning of illness symptoms, compared to only 78% (96/123) of AdV detections ($p < 0.001$). Overall, viral coinfections appeared to be associated with decreased illness severity of symptoms in healthy children attending daycare. Children with multiple viruses detected at the time of illness onset had decreased rates of fever at this time compared to children with a single virus detected (OR: 0.6 ... CI-95%: 0.35, 0.88 ... $p = 0.01$... generalized estimating equations).

Conclusions: A high proportion of respiratory illnesses in daycare attendees had multiple viruses detected during the course of illness. Delay between onset of illness and viral detection varied by virus, indicating that AdV and other viruses may be underrepresented in studies of virus epidemiology that use only a single test at symptom onset.

Abstract No. 41 (Faculty)

Title

Acute illness symptoms associated with primary human bocavirus infection in infants

Affiliations

Wayne State University, Detroit MI
University of Washington and Seattle Children's Research Institute, Seattle WA

Authors

Emily Martin, MPH PhD
Jane Kuypers, PhD
Anna Wald, MD MPH
Janet Englund, MD
Danielle Zerr, MD MPH

Abstract

The role of human bocavirus as a causative agent of disease is not well understood. We have previously documented that this virus can shed from saliva consistently for over a year in young infants, making cross-sectional studies difficult to interpret. We analyzed banked saliva samples and symptom data from children followed from birth up to two years of age with weekly saliva collection and daily symptom diaries of signs and symptoms. Bocavirus DNA was detected by polymerase chain reaction. A case-crossover analysis using conditional logistic regression was performed to evaluate symptoms recorded during the 3 weeks surrounding primary infections, defined as initial detection of bocavirus in the saliva, compared to symptoms occurring 4 to 7 weeks prior to and following primary infection. 87 children were followed from birth for a median of 705 days (range 551 to 778 days). 80 (92%) of 87 had bocavirus detected at least once. Primary infection events lasting at least 1 week were captured in 66 children. Median age at primary infection was 11 months (interquartile range: 7 to 16 months). Acquisition of bocavirus was associated with new onset of coughing (Odds Ratio (OR): 2.35, 95% Confidence Interval (C.I.): 1.20, 4.62 ... $p = 0.01$) and illness visits to the child's physician (OR: 2.63, 95% C.I.: 1.02, 6.82, $p = 0.05$). Presence of fever was also increased, but not significantly (OR: 2.00, 95% C.I.: 0.93, 4.29, $p = 0.08$). Vomiting, diarrhea, and rash were not associated with acquisition. These data provide the most complete longitudinal analysis of

bocavirus acquisition and associated illness available to date, and support the role of primary bocavirus infection as an etiology of acute respiratory illness.

Abstract No. 42 (Faculty)

Title

Exenatide Treatment Effects on Feeding Behavior in Rats: Antagonism by Peripheral, but not Central, Administration of the GLP-1 Receptor Antagonist Exendin 9-39

Affiliations

Department of Pharmacy Practice, EACHPS and Department of Pharmaceutical Sciences, EACHPS

Authors

Nicole R Pinelli, PharmD, MPH, Patrick Dodd, BS, Hassan A Ghoul, PharmD, Lea M Monday, PharmD, Linda A Jaber, PharmD and Randall L. Commissaris, PhD.

Abstract

Purpose: Exenatide is an injectable antihyperglycemic agent approved for the treatment of type 2 diabetes mellitus that works presumably via agonist actions at glucagon like peptide-1 (GLP-1) receptors. GLP-1 receptors are found in both the brain and gut. Previous studies from our laboratory demonstrated that Exenatide reduces feeding behavior in rats, and this effect is antagonized by systemic administration of the GLP-1 antagonist exendin 9-39. The present experiment determined if this effect of Exenatide on feeding behavior is reduced by administration of the exendin 9-39 directly into the central nervous system (CNS) via intracerebroventricular (ICV) administration. **Methods:** Two-hour feeding studies were conducted in male rats that had been food-restricted for 16 hours prior to testing. In the first experiment, Exenatide (2.5 ug/kg)/vehicle and exendin 9-39 (200 ug/kg)/vehicle were administered IP 30 minutes prior to initiation of the feeding test using 45 mg BioServe Pellets. In the second experiment, the effects of this same Exenatide systemic treatment (2.5 ug/kg Exenatide or Vehicle) were determined with and without pretreatment with the antagonist exendin 9-30 administered directly into the CNS via ICV

infusion.

Results: In the first experiment, systemic pretreatment with 200 ug/kg IP exendin 9-39 significantly reduced the effects of 2.5 ug/kg Exenatide IP to reduce feeding behavior. In the second experiment, ICV administration of 100 ug exendin 9-39 directly into the lateral ventricle did not significantly antagonize the effects of Exenatide to reduce feeding behavior.

Conclusions: The present findings (1) replicate previous findings indicating that the effects of Exenatide to reduce feeding behavior are mediated by agonist actions at GLP-1 receptors, and (2) suggest that these effects are NOT mediated by GLP-1 receptors in the CNS.

Abstract No. 43 (Faculty)

Title

Novel Protein-protein Interactions & Protein Phosphorylation in Insulin Signaling

Affiliations

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Authors

Xiangmin Zhang, Geetha Thangiah, PhD, Morgan Zingsheim, MS, Kimberly Pham, Alex Chao, Paul Langlais, PhD, Moulun Luo, PhD, and Zhengping Yi, PhD*

Abstract

Skeletal muscle insulin resistance is one of the earliest abnormalities in individuals with the metabolic syndrome and predisposes to the development of type 2 diabetes (T2D). The insulin signaling pathway is crucial to a wide variety of biological processes in skeletal muscle and involves precise, controlled protein-protein interactions as well as protein phosphorylation to relay the insulin signal. Defects in the insulin signaling pathway have been implicated in the development of skeletal muscle insulin resistance but the precise abnormalities are largely unclear. Insulin receptor

substrate-1 (IRS-1) plays a central role in the insulin signaling cascade and hyper serine/threonine phosphorylation has been considered to be one of the main causes for insulin resistance and T2D. Extensive research has been carried out to study the role of kinases in IRS-1 phosphorylation and insulin action. Little is known about how serine/threonine phosphatases act on IRS-1 and other insulin signaling proteins. The present project was undertaken to discover phosphatases and other novel interacting partners of IRS-1 and to discover novel phosphorylation of proteins in the insulin signaling pathway. Methods used included cell culturing, immunoprecipitation, western blotting, 1D-SDS-PAGE, trypsin digestion, HPLC-ESI-MS/MS, in cell kinase inhibitor assays, protein overexpression and siRNA mediated knock-down, site-specific mutagenesis. Towards this end, proteomics analysis revealed 11 novel endogenous insulin-stimulated IRS-1 interaction partners from L6 myotubes, a well characterized cell model for skeletal muscle insulin signaling (n=5). Protein phosphatase 1 regulatory subunit 12A (PPP1R12A) was among those proteins showing an insulin stimulated increase in association with IRS1. We verified the interaction between endogenous IRS-1 and PPP1R12A by western blot analyses. In cell kinase inhibitor experiments indicated that the interaction of PPP1R12A and protein phosphatase 1 catalytic subunit (PP1c) with IRS1 is dependent upon the activation of AKT and mTOR/Raptor. PPP1R12A protein overexpressing resulted in decreased IRS-1 phosphorylation. Furthermore, in order to study the role of phosphorylation in regulating PPP1R12A activity, we have identified 20 PPP1R12A phosphorylation sites, 5 of which are novel, and obtained quantitative information for 10 phosphorylation sites, including 6 insulin sensitive sites. Additionally, in cells kinase inhibitor assay identified several rapamycin sensitive sites. We have mutated Ser20 and S507 to alanine, respectively, in order to test the hypotheses that pSer20 or pSer507 is required for PP1c activity as well as insulin stimulated interactions between PPP1R12A and IRS-1 or PP1c. In summary, we have discovered novel protein-protein interactions & protein phosphorylation in insulin signaling. The results suggest that PPP1R12A and PP1c are new members of the insulin stimulated IRS-1 signaling complex and the interaction of PPP1R12A/PP1c with IRS1 is dependent upon the activation of AKT and mTOR/raptor. In addition, PPP1R12A is heavily phosphorylated and multiple phosphorylation sites are regulated by insulin and/or mTOR. These results have provided new insights as to how IRS-1 undergoes insulin induced dephosphorylation and how PPP1R12A modulates insulin action. This

information is important for our understanding of the biology of insulin signaling and the complication in insulin action associated with T2D.

Abstract No. 44 (Faculty)

Title

HPLC-ESI-MS/MS Analysis of Protein Phosphatase 1 Regulatory Subunit 12B Phosphorylation

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Authors

Kimberly Pham¹, Paul Langlais¹, Alex Chao¹, Morgan Zingsheim¹, Xiangmin Zhang^{1,2}, and Zhengping Yi^{1,2}

Abstract

Protein phosphatase 1 (PP1) is one of the major phosphatases responsible for protein dephosphorylation in eukaryotes. Protein phosphatase 1 regulatory subunit 12B (PPP1R12B), one of the regulatory subunits of PP1, can bind to the catalytic subunit of PP1, PP1cδ ... , and modulates the specificity and activity of PP1cδ ... against its substrates. Phosphorylation of PPP1R12B on Threonine 646 by Rho-kinase inhibits the activity of PP1c-PPP1R12B complex. However, whether PPP1R12B phosphorylation at Threonine 646 and other sites is regulated by insulin is currently unknown. We set out to identify phosphorylation sites in PPP1R12B, and quantify the effect of insulin on PPP1R12B phosphorylation using HPLC-ESI-MS/MS. 14 PPP1R12B phosphorylation sites were identified, 7 of which were previously unreported. Potential kinases were predicted for these sites. Furthermore, relative quantification of PPP1R12B phosphorylation sites for basal and insulin-treated samples was obtained by peak area-based label-free mass spectrometry of fragment ions. The results indicate that insulin stimulate the phosphorylation of PPP1R12B significantly at Ser29 (2.76 ± 0.64-fold), Ser504 (11.02 ± 2.76-fold), and Ser645/Thr646 (2.52

± 0.49-fold). Results from this study identify PPP1R12B as a phosphatase subunit that undergoes insulin stimulated phosphorylation, suggesting that PPP1R12B plays an as-of-yet undetermined role in insulin signaling.

Abstract No. 45 (Student_Graduate)

Title

Contributions to Patient Care from P3 IPPE Students During an Interprofessional Older Adult Home Visit

Affiliations

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Authors

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Abstract

Objective: To quantify medication use and classify drug related problems (DRPs) discovered by third-year student pharmacists (P3s) during medication reviews performed in older adult homes during interprofessional team visits.

Methods: During an interprofessional collaborative learning experience with second-year medical students, P3s conducted a medication therapy management (MTM) review including a comprehensive medication history and assessment of the older adult's pill box and medication storage in the home. Medication calendars and DRP recommendations were prepared by each P3 and finalized with a pharmacy preceptor. Older adults, who had been recruited from community centers, church groups, and geriatric specialty centers, granted assent to use of their information. During the

second visit or phone call, the P3 explained the recommendations and calendar to the older adult. Two second-year student pharmacists categorized medications and classified severity of DRPs related to medicine benefits and side effects using the Severity of Error in Medication Order scale (AJHP 99;56:2449). Discrepancies were resolved by discussion between the student evaluators. Descriptive statistics were calculated with SPSS version 19.

Results: Eighty older adults used 8.9 ± 3.9 medications (prescriptions, herbals, and over-the-counters; total 711) and had 10.7 ± 5.7 DRPs (range 2-23; total 861). Cardiovascular medications were the most commonly used medications (3.3 ± 1.7 medications). The most common DRP recommendation categories were medicine benefit and side effects (22%), monitoring (19%), patient education (17%), lifestyle (17%), and adherence (16%). The highest DRP subtype was starting an over-the-counter medication for untreated condition. The majority of patient education recommendations were related to immunizations. Most medicine benefit and side effects DRP severities (total 191) were classified as significant (61%) or minor (34%) with 5% of the recommendations considered serious - patients encouraged to see healthcare provider soon.

Conclusions: Student pharmacist involvement in home visit MTM reviews was effective at identifying important DRPs.

Abstract No. 46 (Faculty)

Title

Combining anticancer agents photodynamic therapy and LCL85 leads to enhanced autophagy, selective increases in ceramides, defective apoptosis in the absence of cell death, and long-term sensitization

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3 Alicja Bielawska, Ph.D.

Abstract

Two anticancer agents, LCL85 and photodynamic therapy (PDT) were combined to test whether the combination PDT/LCL85 evokes changes in the sphingolipid profile and promotes cell death in SCCVII mouse squamous carcinoma cells. Short-term treatment of cells with PDT or the combination led to activation of DEVDase in the absence of increases of other apoptotic markers. Concomitantly, PDT/LCL85 induced enhanced autophagy and enhanced levels of C18-, C20-, and C20:1-ceramide, and C18-dihydroceramide. None of the treatments affected short-term viability of cells. In contrast, long-term clonogenic survival was reduced not only after PDT or LCL85, but even more after PDT/LCL85. Overall, our data show that short-term exposure to PDT/LCL85 led to enhanced autophagy with concomitant accumulation of individual ceramides and a dihydroceramide, as well as defective apoptosis without cell death. Long-term exposure to PDT/LCL85 enhanced overall cell killing, supporting translational potential of PDT/LCL85.

Abstract No. 47 ()

Title

Glycogen synthase is phosphorylated at tyrosine 212 and this novel site is insulin stimulated in 3T3-L1 cells

Affiliations

Wayne State University
Arizona State University

Authors

Yifei Wu, Xiangmin Zhang, Paul Langlais, Morgan Zingsheim, Alex Chao, Lawrence J. Mandarino, Kurt Hojlund, and Zhengping Yi

Abstract

Glycogen synthase (GS) converts glucose to glycogen by incorporating uridine diphosphate glucose into glycogen. The muscle isoform of GS, encoded by the GYS1 gene, is the rate-limiting enzyme in glycogen synthesis. Reduced insulin stimulation of glycogen synthesis and impaired activation of glycogen synthase are consistent findings in skeletal muscle in type 2 diabetes. Insulin is known to activate muscle GS by dephosphorylation of at least nine serine residues. Recently, phosphoproteomic studies have suggested additional phosphorylation sites on muscle GS. The present work was set out to investigate the phosphorylation of GYS1 in rat skeletal muscle and 3T3-L1 fibroblasts using HPLC-ESI-MS/MS. We have obtained 48% protein sequence coverage of GYS1 both in rat skeletal muscle and 3T3-L1 fibroblasts. S645 and S647 were identified as phosphorylation sites in rat skeletal muscle. S709 and S711 were identified as phosphorylation sites in 3T3-L1. In 3T3-L1, two additional phosphorylation sites were identified among S717, S718, S719, S721, and T722, although exact localization is currently unavailable. The phosphorylation of T722 has been previously reported, but the other phosphorylation site among S717, S718, S719, and S721 is novel according to our knowledge. Y212, another novel phosphorylation sites, was identified in both rat skeletal muscle and 3T3-L1. As a result, we applied a mass spectrometry based phosphorylation quantification strategy developed in our laboratory to assess the effect of insulin on the phosphorylation of GYS1 at Y212. HPLC-ESI-MS/MS analysis revealed that insulin increased phosphorylation of Y212 by 1.79 ± 0.55 fold compared to basal in 3T3-L1 fibroblasts. Experiments are on-going to investigate whether this site is insulin responsive in L6 myotubes and in vivo in a rat muscle model. In brief, phosphorylation of GYS1 at Y212 is possibly regulated by insulin and may play a role in regulating glucose metabolism. Studies of the phosphorylation of this tyrosine residue in skeletal muscle of insulin resistant individuals may contribute to the understanding of the pathogenesis of type 2 diabetes.

Abstract No. 48 (Post_Doctoral_Fellow)

Title

Evaluation of Standard and High Dose Daptomycin Versus Linezolid Against Vancomycin-Resistant Enterococci in an in vitro Model of Simulated Endocardial Vegetations (SEV)

Affiliations

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Authors

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Abstract

Background: Daptomycin (DAP) displays concentration-dependent pharmacodynamics. DAP minimum inhibitory concentrations (MIC) for enterococci are typically 1-2-fold higher than in *Staphylococcus aureus*. Based on Emax models, higher dosages of DAP may be needed to adequately treat enterococcal infections. We investigated the bactericidal activity of DAP at varying dose exposures vs. linezolid (LZD) against vancomycin-resistant *Enterococcus faecium* (VRE) in an in vitro Pharmacokinetic/Pharmacodynamic (PK/PD) SEV model.

Methods: The killing effects of DAP 6 (D6, Cmax 93.9 mg/L, t_{1/2} 8h), 8 (D8, Cmax 123.3 mg/L), 10 (D10, Cmax 141.1 mg/L), 12 (D12, Cmax 183.7 mg/L) mg/kg/day, AUC 0-24 494-1277 mg*h/L, and LZD 600 mg (Cmax 15.1 mg/L, t_{1/2} 5h) q12h were evaluated against 2 VRE strains (R582 and 09-184D1051) in a 96h in vitro PK/PD SEV model and media supplemented with albumin (3.5 g/dL). Bactericidal and bacteriostatic activity were defined as a ≥ 3 -log₁₀ CFU/g (99.9% decrease) or a < 3 -log₁₀ CFU/g reduction in colony count from the initial inoculum, respectively. Model samples were plated on DAP and LZD-containing agar at 3-fold the MIC for detection of resistance.

Results: Against VRE R582 (DAP MIC = 4 mg/L, LZD MIC = 2 mg/L) and 09-184D1051 (DAP MIC = 2 mg/L, LZD MIC = 16 mg/L), D10 and D12 displayed sustained bactericidal activity at 96 h. For

R582, D10 and D12 were more efficacious at decreasing log₁₀ CFU/g than D6, D8, and LZD at 96h ($p \leq 0.012$), and D12 significantly greater than D10 (72-96h, $p < 0.001$). Against 09-184D1051, D10 and D12 had significantly greater reduction in colony counts than D6, D8 and LZD (24-96h, $p < 0.012$). LZD was bacteriostatic against R582 and displayed no activity against 09-184D1051. No mutants were recovered.

Conclusions: DAP displayed a dose-dependent response against 2 VRE strains. High dose DAP (D10 and D12) had a more optimized pharmacodynamic profile producing bactericidal activity against VRE. Further research is warranted.

Abstract No. 49 (Faculty)

Title

The Atypicals: Unexpected Outcomes in Children

Affiliations

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Authors

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Abstract

BACKGROUND: Atypical antipsychotic prescriptions for pediatrics increased 10-fold since 2007. NPDS single substance atypical exposure in patients less than 19 years of age increased 8% from 2007 -2009, while overall exposures in this age group increased 0.4%. Frequency and type of adverse effects associated with pediatric use in therapeutic and overdose scenarios is not well known.

OBJECTIVE: To estimate the frequency and type of atypical antipsychotic exposure in children and associated adverse effect, dose-relationship, and outcomes.

DESIGN/METHODS: Retrospective analysis of

patient exposures reported to a regional poison center. Inclusion criteria were age 2 to <19 years (yrs) as of January 1, 2010, single agent exposure to an atypical antipsychotic, medical outcome of minor, moderate, and date of exposure 2010. Cases not followed or reported no effects from exposure were excluded. Descriptive analyses were conducted using Chi-Square Fisher's Exact and student's t-tests. RESULTS: A total of 135 cases met criteria. The sample had mean age 10.8 ± 6.6 yrs ... 0.8-18 yrs) with 51% female. Pre-morbid conditions were common, including depression 22%, bipolar 18%, ADHD 9%, substance abuse 5%, and previous suicide 3%. Atypical antipsychotic agents were: quetiapine 43%, aripiprazole 20%, risperidone 13%, olanzapine 11%, ziprasidone 11%, clozapine 1%, iloperidone 1%. Intent was self-harm (43.7%), accidental poisoning (37%), abuse (6%), therapeutic error (3.7%), intentional misuse (1.5%), and ADR (3%). Children with self-harm were older than those with accidental poisoning (16 ± 1.4 v 2.8 ± 2.0 years ... $p < .001$). Mechanical ventilation most frequently associated with quetiapine (10%) and ziprasidone (14%). ICU admission was more common with quetiapine (27%) and aripiprazole (26%). Prolonged QTc (defined as > 450 msec) occurred in 22 cases. Overall, outcomes were 52% mild, 41% moderate and 5% major (2 ziprasidone and 5 quetiapine). Moderate outcomes were reported in 8 children with history of less than AAPCC triage dose exposure. CONCLUSIONS: Frequency of poisoning exposures to atypical antipsychotics in children reported to a regional poison center reflected clinical use of these agents according to marketing data. Quetiapine represented the most exposures, highest severity of outcomes, and need for ICU admission. AAPCC published triage data predicted major outcomes, but was not sensitive enough to exclude moderate outcomes. NPDS reported exposures to antipsychotics and self-harm for this age are increasing. Dose related toxicity data for pediatrics may require a prospective study with a larger sample.

Abstract No. 50 (Faculty)

Title

Meningococcal Meningitis Among Children in China, South Korea, and VietNam, 1999-2002

Affiliations

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Authors

Soon Ae Kim, PhD, Dong Wook Kim, PhD, Dang Duc Anh, PhD, Jung Soo Kim, MD, Bai Qing Dong, MD, Paul E. Kilgore, MD

Abstract

Background. *Neisseria meningitidis* (Nm) is an important cause of invasive bacterial disease. We analyzed the cerebrospinal fluid (CSF) specimens collected from children admitted with symptoms of invasive bacterial meningitis in China, South Korea, and VietNam to better understand epidemiologic patterns of meningococcal infection in Asian children.

Methods. We performed retrospective analysis of CSF samples collected during active, prospective, population-based surveillance among children aged <5 years old in Hanoi, VietNam (1999-2001), Jeonbuk Province, South Korea (2000-2002), and Nanning, China (2000-2002). CSF specimens were tested by PCR, and were further tested by Nm serogrouping PCR.

Results. Among the 2,032 CSF specimens tested, 284 (14%) were Nm PCR-positive, including 67 out of 587 (11%) from China, 92 out of 697 (13%) from Korea, and 125 out of 878 (14%) from VietNam. More than 50% of cases were observed in neonates and infants aged <6 months old. Among the Nm PCR-positives (ctrA), 44 (15.5%) were serogrouped, out of which 2 (5%) was serogroup B, 21 (48%) were C, 12 (27%) were X, and 9 (20%) were Y.

Conclusions. These results suggest that Nm in Asia occurs in young infants as well as older children. Improvements in national surveillance are required to

better understand NIDDM disease burden in all age groups across Asia.

Abstract No. 51 (Student_Graduate)

Title

Effects of hemodialysis on glycemic control in hospitalized type 2 DM patients receiving basal-bolus insulin: A retrospective chart review

Affiliations

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Authors

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Francine Salinitri, PharmD
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Abstract

Diabetes is one of the leading causes of end stage renal disease (ESRD) resulting in hemodialysis and there is limited data on the proper insulin regimen used to manage hyperglycemia in patients with renal failure and Type 2 Diabetes Mellitus (T2DM). Recent data has indicated that optimizing the basal-bolus insulin regimen improves glycemic control in chronic kidney disease (CKD) patients on hemodialysis. It has also been reported that patients with T2DM and ESRD requiring hemodialysis experience greater variability in their blood glucose levels. The purpose of this study is to measure the effect of hemodialysis on blood glucose levels and insulin requirements. This study is a retrospective time series cohort study. It consists of a chart review of patients diagnosed with Type 2 Diabetes Mellitus and ESRD requiring hemodialysis and receiving basal-bolus insulin therapy. The basal-bolus insulin therapy consists of a short acting and long acting insulin per hospital protocol without modification to the standing orders for the duration of the study period. Data collected includes baseline demographic data consisting of age, gender, weight, and race/ethnicity, past medical history, reason for admission, point-of-care glucose records, insulin

administration records, and the hemodialysis records. The primary outcome is to measure the effect of hemodialysis on blood glucose levels. Outcomes are evaluated at dialysis day -1, day 0 and day 1, in which with day -1 is defined as the day prior to the hemodialysis treatment, day 0 is defined as the day of hemodialysis treatment and day 1 is defined as the first day post-hemodialysis. A re-challenge of day -1, day 0 and day 1 will be performed in patients with at least two eligible hemodialysis session time series and still meet all inclusion/exclusion criteria. A repeated-measures ANOVA/ANCOVA will be used to analyze mean glucose and insulin requirements. A McNemar test will be used to analyze hypoglycemia rates and glucose >300 mg/dL.

Abstract No. 52 (Faculty)

Title

Health Risks and Outcomes of U.S. Black Abused and Non-Abused Women

Affiliations

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College of Pharmacy and Health Sciences

Authors

Krim K. Lacey

Abstract

Intimate partner violence is a serious public health problem that has devastating effects on the well-being of women in the United States. The impact of intimate partner violence may be felt more severely by Black women who are found to have higher rates of intimate victimization and negative outcomes (e.g. deaths) in comparison to women of other racial/ethnic groups. The increase in violence against black women, attributed to their lower social status in the U.S., may further predispose them to both short and long-term health consequences. Despite their vulnerability to these outcomes, limited probability studies have examined the effects on the health and well-being of U.S. Black women. The current research addresses the relationship between intimate partner violence and physical and mental health. The study further aims to understand the difference in health consequences between abused and non-abused

women. Data from the Collaborative Psychiatric Epidemiology Survey (CPES) collected between 2001 and 2003, with a slightly modified version of the World Health Organization Composite International Interview were used. Preliminary findings revealed that abused Black women were at risk for both physical and mental health consequences. Rates of physical and mental health disorders were also significantly higher for abused women in comparison to non-abused women.

Abstract No. 53 ()

Title

Loop-mediated Isothermal Amplification for Detecting *Streptococcus pneumoniae* in Cerebrospinal Fluid.

Affiliations

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Authors

Mitsuko Seki, Paul E. Kilgore, Eun Jin Kim, Soon Ae Kim, Dong Wook Kim

Abstract

Background. *Streptococcus pneumoniae* and other invasive bacteria are leading causes of meningitis in developing countries. A novel loop-mediated isothermal amplification (LAMP) utilizes a unique priming mechanism that yields specific DNA products in a shorter period of time than PCR. The availability of the LAMP method offers the opportunity to develop a novel assay for detection of *S. pneumoniae* that is more reliable and easier to perform than bacterial culture and PCR-based assays. We established and evaluated the LAMP assay for *S. pneumoniae* (Sp-LAMP) and compared its performance using cerebrospinal fluid (CSF) specimens collected from patients with suspected meningitis.

Methods. We established the Sp-LAMP assay targeting the *lytA* gene. The detection limit and analytical specificity of Sp-LAMP reaction were assessed and Sp-LAMP products were analyzed. Moreover, we evaluated the Sp-LAMP assay using a set of 106 randomly selected CSF specimens from children with suspected meningitis collected between 1998 and 2002 in Vietnam (n=33), China (n=33) and Korea (n=40).

Results.

The primer specificity was validated using 10 *Streptococcus* and seven non-*Streptococcus* species. Within 30 minutes, the assay could detect 10 or more copies of purified *S. pneumoniae* DNA with a sensitivity 1,000 times that of conventional PCR. The LAMP method proved to be more sensitive than previously described PCR methods when using CSF samples (33 CSF were positive by LAMP vs. 18 by PCR). The detection rate of the LAMP method was substantially higher than those of the PCR, culture and latex agglutination methods. In this small sample, relative to the LAMP assay, clinical sensitivities of PCR, culture and latex agglutination tests were 54.5, 33.3 and 15.2%, respectively ... while clinical specificities of three methods were 100%.

Conclusions.

1. We have successfully established a LAMP-based *S. pneumoniae* DNA amplification method and confirmed that its analytical specificity is high and its detection limit is low.
 2. Compared to PCR-based detection methods, this assay allows the detection of *S. pneumoniae* from both spiked CSF specimens and clinical CSF specimens with higher analytical and clinical sensitivity.
 3. Because the LAMP reaction is easy to set up and does not require special equipment, it has obvious advantages in clinical settings and in population-based studies with limited access to well-equipped laboratories.
 4. Further development and evaluation of the Sp-LAMP will enhance the global diagnostic capability for *S. pneumoniae* detection.
-

Abstract No. 54 (Student_Undergrad)

Title

Specialized Instrumentation Used in the Analysis of Sitting Posture

Affiliations

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Authors

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Abstract

INTRODUCTION: Neck pain has been attributed to poor sitting postures that are, in part, due to increased compression or tension of structures resulting from inefficient muscle activations. However, the contribution of muscle activity to seated postures has not been fully integrated into treatment approaches and postural re-education programs despite the crucial role muscles play in maintaining one's posture and providing movement-related proprioceptive feedback. The purpose of this presentation is to highlight the methods used to quantify the relationship between muscle activity in two sitting postures. **METHODS:** Middle-aged adults will be asked to perform two sitting tasks. For the first task, participants will sit in their normal posture. For the second task, participants will sit in their "best posture". Prior to recording performance data, the average of three maximum voluntary isometric contractions will be used to normalize EMG activity for each muscle tested. **INSTRUMENTATION:** Wireless EMG sensors will be placed bilaterally on eight muscles located in the cervical, thoracic and lumbar regions. Data will be recorded using the TeleMyo 2400T™ DTS Telemetry system. Position data corresponding to each posture will be simultaneously collected using the Optotrak Certus® motion capture system. **DISCUSSION:** Specialized instrumentation permits precise measurement of corresponding movements and activities that may uncover how poor posture contributes to neck pain. Therapists may use this information to develop new treatment interventions and enhance postural re-education programs. Moreover, the use of specialized instrumentation may complement traditional assessments thus offering researchers and students

numerous opportunities to enhance clinical outcome measures. **ACKNOWLEDGEMENTS:** FRAP II Award and D.E. Adamo

Abstract No. 55 (Student_Graduate)

Title

Comparison of standard versus prolonged-infusion of doripenem for the treatment of various infections.

Affiliations

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Authors

Lama Hsaiky PharmD., B.C.P.S. ... Kyle Murray, PharmD. ... Lianne Kokoska, Pharmacy Student ... Raymond Cha, PharmD.

Abstract

Background: Doripenem (DOR) is the most recently approved carbapenem, and features a broad spectrum of activity against many organisms. In vitro studies have demonstrated that the antimicrobial activities of carbapenems are optimized by maintaining the concentration above the minimum inhibitory concentration for greater than 40% of the dosing interval. Available literature evaluating DOR prolonged infusions for the treatment of resistant organisms is largely limited to in vitro modeling or pharmacodynamic Bayesian simulations. While these data appear promising, clinical data comparing traditional dosing of DOR (1 hour) versus prolonged infusion (4 hours) is essential.

Methods: We conducted a retrospective analysis of 61 patients receiving DOR 1-h vs. 4-h infusion for at least 72 hours between May 1st 2009 and May 30th 2010. Standard dosing recommendations were from the manufacturer's labeling and extended dosing was based on published literature. Adjustments to dosage and/or frequency were made based upon renal function according to these recommendations. Baseline demographics included mean age, ICU residence, hospitalization or antimicrobials in previous 90 days and mean APACHE-II scores. Infection characteristics included indicated disease,

organism and imipenem MIC. Outcomes evaluated include mean length of stay (LOS) following initiation of DOR, microbiological eradication in the microbiologically evaluable population, 30 day mortality, and clinical outcome which was categorized as clinical failure and clinical cure or improvement according to previously published trials.

Results: 61 patients treated with DOR were included in the analysis. 30 received the 4-hour infusion, and 31 received the 1-hour infusion. There were no statistically significant differences in baseline demographics and infection characteristics between the two groups. Predominant infections included pneumonia, urinary tract infections, bacteremia, and intra-abdominal infections. The mean LOS following initiation of DOR was 16.9 and 12.7 for the DOR 1-h and 4-h groups respectively ($p=0.205$). Four (12.9%) DOR 1-h patients and 5 (16.7%) 4-h patients died within 30 days of discharge ($p=0.678$). 21/31 DOR 1-h and 21/30 4-h patients were microbiologically evaluable ($p=0.85$) of which 17 (81%) DOR 1-h and 13 (62%) 4-h patients achieved microbiological eradication ($p=0.172$). 24/31 DOR 1-h and 24/30 DOR 4-h patients achieved a favorable clinical outcome ($p=0.805$).

Conclusion: Prolonging the DOR infusion duration to 4 hours did not lead to significant differences in LOS, all cause 30 day mortality, microbiological eradication rates, or favorable clinical outcomes in our study population. Although this was a relatively small retrospective evaluation, our results indicate that clinicians should exercise caution when considering the standardization of DOR dosing to prolonged-infusion. More extensive prospective clinical studies comparing prolonged infusion to standard infusion rates are needed before recommending routine use of prolonged administration.

Abstract No. 56 (Faculty)

Title

SHORT TERM EFFECTS OF AN EDUCATIONAL PROGRAM ON KNOWLEDGE AND SELF-REPORTED BEHAVIOR CHANGE IN PATIENTS WITH KNEE OSTEOARTHRITIS.

Affiliations

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Wayne State University

Authors

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Heilman D'Andra, Rowley Kara, Li Jia

Abstract

SHORT TERM EFFECTS OF AN EDUCATIONAL PROGRAM ON KNOWLEDGE AND SELF-REPORTED BEHAVIOR CHANGE IN PATIENTS WITH KNEE OSTEOARTHRITIS. Schiller M, Carreira J, Heilman D, Rowley K, Li J. Wayne State University, Detroit, Michigan.

INTRODUCTION: Previous investigations have shown the benefits of group educational programs for people with knee osteoarthritis (OA). Goal setting has also been shown to increase health related behavioral changes. The purpose of this study was to determine the short-term effects of an educational program and whether goal setting influenced knowledge and self-reported behavior change in patients with knee OA. Specific goals were to: 1) determine if a 2-hour educational program was effective in gaining knowledge and to see if the knowledge was retained 2) to demonstrate if active goal setting had an impact on behavioral changes 3) to see what behaviors, if any, were changed.

METHODS: A prospective, randomized intervention study was used. Two hour classes were provided to 125 participants by a PT. 86 consented to participate in the study. The participants were randomized into goal setting (GS) and non-goal setting (NGS) groups. Participants then completed a written multiple-choice pre-test regarding knee OA. Both groups were given a post-test identical to the pre-test at the conclusion of the class. The GS group was asked to write a goal at the end of the program. Participants were contacted by phone 3-4 weeks after the program and were asked the same test questions. They reported on any

behavioral changes made since having attended the course. Data collected included test scores and qualitative data of behavioral changes. In addition, participants in the GS group were asked to recall their goal. Data analysis included the Wilcoxon Signed Rank, Mann Whitney, and Pearson's Chi-squared tests. RESULTS: Of the 86 participants, 16 were unavailable for follow-up and 73(41 from GS and 32 from NGS) completed all pre-, post-, and follow-up data. A significant difference was found between pre- and post-test scores ($p < 0.0001$). No significant differences were found with the post-test to follow-up ($p = 0.4618$). Self-determined goals did not result in further retention or greater behavioral changes. 91% of participants contacted at follow-up indicated they had made changes as a result of having attended the class. Of those that reported changes, 64% changed their activity level, 63% began exercise, 56% used ice/heat and 37% initiated weight management strategies. DISCUSSION: Previous investigations have studied knowledge and exercise over longer periods for knowledge and motivational gains. This study has shown cognitive benefits and behavior changes from a single 2 hour educational class. Goal setting theories suggest that specific and directed goals may lead to more behavioral changes. This study incorporated a goal-setting strategy that was non-specific and may explain why goal writing in this study did not produce significant results. CONCLUSIONS: The study results indicate that as a result of attending a one-time knee OA educational program, knowledge was gained and maintained over a short-term period. Behavioral changes were made, but goal writing did not produce increased behavior changes.

Abstract No. 57 (Student_Graduate)

Title

Betulinic acid inhibits activity of 20S proteasome and potentiates methamphetamine-induced toxicity in rat striatal synaptosomes

Affiliations

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Authors

Bryan A. Killinger, Jessica Zilberberg, and Anna Moszczynska

Abstract

In experimental animals, high doses of a psychostimulant methamphetamine (METH) produce a loss of dopamine (DA) and serotonin (5-HT) nerve terminals in the striatum. Several molecular mechanisms are involved in toxicity of METH to these terminals, including oxidative stress, inflammation, apoptosis and changes to proteasomal function. Proteins damaged by oxidative stress are degraded by the 26S proteasome, which consists of the 20S catalytic core and two 19S regulatory caps. The role of the proteasome in neurodegeneration is controversial. Dysfunction of 20S activity can lead to neurotoxicity. On the other hand, there is evidence that mild inhibition of the 20S can protect nerve cells from a variety of insults. Betulinic acid (BA) is well known as an anti-cancer agent with no or minimal toxicity to normal cells. In cancer cells, antitumor activity of BA is mediated by induction of apoptosis and cell cycle arrest. Interestingly, in non-cancer cells, BA treatment was found to protect against oxidative stress and inflammation. As BA can affect mechanisms mediating METH neurotoxicity, the present study was aimed to examine the effects of BA on chymotrypsin-like activity of 20S proteasome and to determine whether BA attenuates or potentiates METH neurotoxicity to DA and 5-HT terminals in striatal synaptosomes of adult Sprague-Dawley rats. As compared to control rats, pre-treatment with BA (50 mg/kg, i.p., 3 h before METH) caused a mild decrease in chymotrypsin-like activity at 1 h after a high-dose binge METH administration (4 x 10 mg/kg, 2 h apart, i.p.) and potentiated METH-neurotoxicity. The results suggest that BA potentiates METH neurotoxicity in vivo via inhibition of chymotrypsin-like activity of 20S proteasome and, potentially, via apoptosis. This work was supported by NIH grant DA023085

Abstract No. 58 (Post_Doctoral_Fellow)

Title

Develop and Synthesis of Inhibitors of N5-Carboxyaminoimidazole Ribonucleotide Synthetase and Mutase for the Treatment of Infective Endocarditis

Affiliations

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Authors

Shahid Islam and Steven M. Firestine

Abstract

Fungal infective endocarditis (IE) is a serious cardiac disease that is associated with a high mortality (60-100%). Traditional antifungal agents are expensive, limited in numbers, and have limited success in the treatment of fungal IE. Newer agents suffer from problems such as toxicity, drug-drug incompatibility or lack of efficacy against some pathogenic fungi. Therefore, there is a critical need for new targets and strategies in antifungal therapy. Our approach is to prepare a variety of inhibitors that will selectively target the enzymes N5-carboxyaminoimidazole ribonucleotide (N5-CAIR) synthetase and N5-CAIR mutase. These enzymes catalyze the sixth and seventh step of the de novo purine biosynthesis in fungi ... however, these enzymes are not required for purine biosynthesis in humans. The difference between human and fungal purine biosynthesis suggests that these enzymes are ideal targets for drug development. Previously, our group has synthesized a variety of nucleotide analogs related to 5-aminoimidazole ribonucleotide (AIR) and carboxyaminoimidazole ribonucleotide (CAIR) and examined their ability to inhibit these enzymes. Given the poor bioavailability of nucleotides, we began to investigate a variety of non-nucleotide analogs of these lead compounds to gain improvements in potency, selectivity and bioavailability. Our initial focus was on imidazole based compounds in which the 5'-ribose phosphate was replaced by a variety of groups which place a carboxylic acid into the phosphate binding pocket. Here we present our design, synthesis and evaluation

of these compounds for their ability to inhibit N5-CAIR synthetase and mutase.

Abstract No. 59 (Faculty)

Title

Evaluation of combination drug treatment for *C. difficile*-associated diarrhea

Affiliations

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Authors

Raymond Cha 1,2, Rebecca Socaciu 2, Joseph Granata 2, Lama Hsaiky 1

Abstract

C. difficile infection is the leading infectious cause of hospital-associated diarrhea in acute care settings. Acute fulminant infection has a high rate of morbidity with an estimated case-fatality rate of >2%. Current SHEA-IDSA guidelines recommend the use of oral (PO) vancomycin plus intravenous (IV) metronidazole for the treatment of severe, complicated CDI (CIII level of evidence), however there is limited clinical data to support any combination therapy. The overall study design is a retrospective analysis evaluating three study groups: PO metronidazole monotherapy versus PO vancomycin monotherapy versus the combination therapy of IV metronidazole and PO vancomycin. 400-500 patients will be identified between May 2009 to February 2011 using electronic records based on positive *C. difficile* culture or diagnosis. Inclusion criteria encompasses a positive *C. difficile* antigen and PCR test and treatment for >72 hours. Exclusion criteria include pregnancy and inflammatory diseases. Demographic assessment includes antimicrobial history, age, comorbidities, and CDI severity. Assessment of treatment safety and efficacy will be evaluated: CDI infection parameters including stool quantification, concurrent antibiotic use, supportive therapy, need for additional therapy, surgical intervention and CDI-associated mortality. At the conclusion of our study, we plan to determine

whether double coverage for *C. difficile* associated diarrhea is statistically advantaged over monotherapy treatment. Preliminary results will be presented.

Abstract No. 60 (Post_Doctoral_Fellow)

Title

Evaluation of Ceftaroline (CPT) activity versus Vancomycin (VAN) against heteroresistant vancomycin intermediate *S. aureus* (hVISA) and VISA methicillin-resistant *Staphylococcus aureus* (MRSA) strains in an in-vitro pharmacokinetic/pharmacodynamic model.

Affiliations

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Authors

Brian Werth, PharmD 1, Molly Steed, PharmD 1, Glenn W. Kaatz, MD 2,3,4, Michael J. Rybak, PharmD, MPH 1,3

Abstract

Background: Ceftaroline is an advanced generation cephalosporin with anti-MRSA activity that was recently approved by the United States Food and Drug Administration (FDA). Ceftaroline binds to penicillin binding proteins (PBP) leading to inhibition of cell wall synthesis and has strong affinity for PBPs 1-3 including the mutated PBP2a, which confers methicillin resistance. Data from our laboratory experiments evaluating ceftaroline's activity against *S. aureus* in a hollow fiber PK/PD model suggest that ceftaroline may exhibit enhanced activity against isolates with reduced susceptibility to vancomycin such as hVISA and VISA. The previously described "seesaw" effect in MRSA in which isolates demonstrate increased oxacillin susceptibility as vancomycin and daptomycin susceptibility decrease may contribute to the enhanced bactericidal activity of ceftaroline against hVISA and VISA isolates. To further explore this relationship a previously described, in-vitro, hollow

fiber PK/PD model was used to compare the activity of vancomycin and ceftaroline against 3 isogenic clinical MRSA/VISA strain pairs.

Methods: Each model was inoculated with 10⁷ CFU/ml of bacteria. Ceftaroline 600mg every 12 hours (f[C_{max}] 15.2 µg/ml) and vancomycin 1g every 12 hours (f[C_{max}] 18 µg/ml) were evaluated. Bactericidal and bacteriostatic activity were defined as a $\geq 3\text{-log}_{10}$ CFU/g (99.9% decrease) or a $< 3\text{-log}_{10}$ CFU/g reduction in colony count from the initial inoculum, respectively. Samples were plated on media containing 3 times the MIC of each antimicrobial to monitor for development of resistance at multiple timepoints.

Results: Ceftaroline demonstrated bactericidal activity against both JH1 (VAN MIC 1, CPT MIC 0.5) and JH9 (VAN MIC 8, CPT MIC 0.5) with a maximum log CFU reduction from baseline of -3.89 and -4.02 respectively. Vancomycin was not bactericidal against either strain. Other results are pending.

Conclusions: Preliminary data from this model has demonstrated that ceftaroline exhibited similar killing profiles against one VISA strain and its MRSA parent and resulted in greater log CFU reduction than vancomycin. Based on previous data, we expected that ceftaroline would have enhanced activity against the VISA strain over the MRSA parent. A possible explanation for this finding may relate to the fact that both of these strains are susceptible to daptomycin. Other investigators have shown that daptomycin non-susceptibility is also associated with enhanced beta-lactam activity. The remaining VISA strains to be evaluated are daptomycin non-susceptible, which may contribute to the enhanced activity of ceftaroline that has been observed in other experiments.

Abstract No. 61 (Post_Doctoral_Fellow)

Title

Clinical Outcomes in Patients with Vancomycin Heteroresistant *Staphylococcus aureus*.

Affiliations

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Abstract

Purpose: Vancomycin has been the primary treatment for infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Selective pressure of relying on vancomycin has led to non-susceptible strains such as vancomycin intermediate *S. aureus* (VISA), vancomycin resistant *S. aureus* (VRSA) and heterogeneous vancomycin intermediate *S. aureus* (hVISA). Heteroresistance to vancomycin is generally undetected by conventional susceptibility methods and treatment with vancomycin has led to unfavorable outcomes such as prolonged bacteremia, vancomycin failure and increased hospital length of stay. The primary objective of this study was to assess the outcomes of patients with infections caused by hVISA treated with vancomycin compared (case matched 1:1) to patients with infections caused by fully vancomycin susceptible MRSA. In addition, the secondary objectives were to assess the

correlation of success or failure on the basis of organism characteristics such as vancomycin susceptibility, SCCmec type, accessory gene regulator (AGR) polymorphism and function, antibiotic tolerance to vancomycin and serum trough concentrations.

Methods: Multicenter retrospective case matched study reviewing clinical *S. aureus* blood and lung isolates obtained in patients. Confirmation of hVISA was done by macro E-test and population analysis profile. Genetic characteristics were identified using multiplex PCR and agr group-specified primers. Patient with hVISA were matched 1:1 to non-hVISA patients based on age, infection source and year of infection.

Results: Pending, will be evaluating patients outcomes comparing patients with hVISA and non-hVISA e.g., mortality, length of stay, source of bacteremia, duration of bacteremia, duration of vancomycin, and previous exposure to vancomycin. We will also characterize outcomes based on organism characteristics e.g., vancomycin minimum inhibitory concentration (MIC) \leq ... or >1 mg/L, vancomycin area under the curve (AUC₂₄) to MIC ratio $<$ or \geq ... 400, and other genotypic characteristics.

Conclusion: Pending.

Abstract No. 62 (Student_Graduate)

Title

Exposing High School Students to Clinical Pharmacy Practice Through Case Based Team Learning

Affiliations

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Authors

Kaitlyn Ross, PharmD candidate 2012 ... Kathryn Morbitzer PharmD candidate 2012 ... Francine Salinitri PharmD

finding the information and answering the questions throughout the case via an interactive team-based approach with a local pharmacist in attendance as a facilitator. The final component of the program is a clinical skills competition between all participating teams, which encompasses the core elements found in previous cases. Upon program enrollment and program conclusion, students will be required to complete a pre-survey, followed by an identical post-survey, regarding their current perceptions of pharmacy and their desired career path. Descriptive statistics will be used to analyze the survey results.

Abstract

According to the American Association of Colleges of Pharmacy (AACP), the demand for pharmacists has increased due to the rapid growth of the healthcare and pharmaceutical industries. With this comes a diverse opportunity in pharmacy careers. In addition, the role of the pharmacist will continue to evolve as the American Society of Health-System Pharmacists (ASHP) implements the Pharmacy Practice Model Initiative (PPMI). As a result, colleges of pharmacy are undergoing curricular changes guided by the Accreditation Council for Pharmacy Education (ACPE) in order to prepare future pharmacists for a larger role in drug therapy management. This requires new recruitment strategies to inform potential students on the changing profession of pharmacy. The aim of this study is to increase student knowledge of the pharmacy profession through active participation in simulated patient cases that are encountered by pharmacists daily. Participation will allow students to understand the complexities of the health care field and broaden the students' understanding of the pharmacy profession. An informational packet will be sent to all high schools within the Greater Essex County District School Board and the Windsor Essex Catholic District School Board. Student teams that consist of grade 11 and 12 students will represent each participating high school. The program consists of two clinical cases that will be provided to the students to emphasize two different areas of pharmacy practice. Students will be responsible for

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