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Childhood obesity: A profile of measures of executive functions, emotional processing, and inflammation

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OBJECTIVES/SPECIFIC AIMS: Childhood obesity has become an issue of some concern worldwide. Some reviews and a recent study in adults have indicated that obesity-related inflammatory responses produce brain damage. However, studies exploring associations between inflammation and executive functions in children are overlooked. Therefore, the objective of this cross-sectional study is to determine whether difficulties in executive functions and emotional processing are associated with obesity and inflammation. METHODS/STUDY POPULATION: We have recruited 12 of a total of 60 children aged 6–8 years old. They have completed the NIH Toolbox Cognition Battery and the NEPSY II Affect Recognition tests. Samples of plasma and saliva were collected to quantify inflammatory biomarkers cytokines (IL-6 and TNF-α) assay by Luminex procedure. We performed descriptive analysis and Mann-Whitney *U* test to compare obese Versus nonobese groups. RESULTS/ANTICIPATED RESULTS: Obese children have lower scores in measures of affect recognition than healthy weight children. They also showed higher median scores in both salivary and plasma IL-6 and TNF-α. DISCUSSION/SIGNIFICANCE OF IMPACT: Although no statistical differences were found among groups in either measurement, these preliminary data based on the initial recruitment suggest that children with higher body mass index may have difficulties in emotional processing. More data will be available after completing recruitment to determine if the association between obesity and affect recognition is significant and if it is mediated by inflammation.

CLINICAL TRIAL

2043

Pharmacokinetic prediction of paclitaxel-induced peripheral neuropathy

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OBJECTIVES/SPECIFIC AIMS: Peripheral neuropathy is the dose limiting toxicity of paclitaxel treatment. Paclitaxel pharmacokinetics (PK), specifically the Cmax and amount of time the concentration remains above 0.05 μM (Tc > 0.05), have been associated with occurrence of severe, clinician-documented neuropathy. The objective of this study was to confirm that paclitaxel PK predicts progression of patient-reported neuropathy. METHODS/STUDY POPULATION: This observational trial enrolled breast cancer patients receiving weekly 1-hour paclitaxel infusions (80 mg/m^2 × 12 cycles) at the University of Michigan Comprehensive Cancer Center. Paclitaxel concentration was measured via LC/MS in plasma samples collected at the end of (Cmax) and 16–24 hours after (Tc > 0.05) first infusion. Patient-reported neuropathy was collected (EORTC CIPN20) at baseline and each cycle. The rate of neuropathy severity increase per treatment cycle is being modeled for each patient. Cmax and Tc > 0.05 values will be introduced into the model to confirm that PK independently contributes to neuropathy progression. RESULTS/ANTICIPATED RESULTS: PK and neuropathy data have been collected from 60 patients for ongoing analysis. Our initial model will characterize the expected severity of neuropathy after each cycle of paclitaxel treatment. The PK-neuropathy model will include either PK parameter to validate their contribution to the progression of neuropathy severity during treatment. We anticipate, based on our preliminary analysis of the first 16 patients, that both PK parameters will significantly contribute to the model but Tc > 0.05 will be more strongly associated with neuropathy progression. DISCUSSION/SIGNIFICANCE OF IMPACT: This project will generate a model that can be used to predict a patient's neuropathy severity throughout treatment using a single, conveniently collected and easily measured PK sample during their first cycle. The next steps of this project include identifying genetic and metabolomic biomarkers that predict which patients experienced more severe neuropathy than would be anticipated based on their paclitaxel PK, and a planned interventional trial of personalized paclitaxel dosing to enhance efficacy and/or prevent neuropathy.

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Fecal bile acids, fecal short-chain fatty acids and the intestinal microbiota in patients with irritable bowel syndrome (IBS) and control volunteers

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OBJECTIVES/SPECIFIC AIMS: Recent data suggest that fecal microbiota and intraluminal organic acids may play an important role in irritable bowel syndrome (IBS) pathogenesis through effects on intestinal secretion and motility. Understanding their contribution will be critical in developing diagnostic and treatment strategies. Objectives and goals of this study will be to: (1) compare fecal microbiota and fecal organic acids in IBS patients and controls and (2) investigate the association between colonic transit and fecal microbiota in IBS patients and controls. METHODS/STUDY POPULATION: We propose a prospective investigation of fecal organic acids, colonic transit and fecal microbiota in 36 IBS patients and 18 healthy controls. The target population will be adults ages 18–65 years meeting Rome IV criteria for IBS (both diarrhea predominant and constipation-predominant, IBS-D, and IBS-C) and asymptomatic controls. Exclusion criteria are: (a) history of microscopic colitis, inflammatory bowel disease, celiac disease, cancer, chronic infectious disease, immunodeficiency, uncontrolled thyroid disease, liver disease, or elevated AST/ALT > 2.0 x the upper limit of normal, (b) prior radiation therapy of the abdomen or abdominal surgeries with the exception of appendectomy or cholecystectomy > 6 months before study initiation, (c) ingestion of prescription, over the counter, or herbal medications affecting gastrointestinal transit or study interpretation within 6 months of study initiation for controls or within 2 days before study initiation for IBS patients, (d) pregnant females, (e) antibiotic usage within 3 months prior to study participation, (f) prebiotic or probiotic usage within the 2 weeks prior to study initiation, (g) tobacco users. Primary outcomes will be fecal bile acid excretion and profile, short-chain fatty acid (SCFA) excretion and profile, colonic transit, and fecal microbiota. Secondary outcomes will be stool characteristics based on responses to validated bowel diaries. Stool samples will be collected from participants during the last 2 days of a 4-day 100-g fat diet and split into 3 samples for fecal microbiota, SCFA, and bile acid analysis and frozen. Frozen aliquots will be shipped to the Metabolite Profiling Facility at Purdue University and the Mayo Clinic Department of Laboratory Medicine and Pathology for SCFA and bile acid measurements, respectively. Analysis of fecal microbiota will be performed in the research laboratory of Dr. David Nelson in collaboration with bioinformatics expertise affiliated with the Nelson lab. Colonic transit time will be measured with the previously validated method using radio-opaque markers. Generalized linear models will be used as the analysis framework for comparing study endpoints among groups. RESULTS/ANTICIPATED RESULTS: This study seeks to examine the innovative concept that specific microbial signatures are associated with increased fecal excretion of organic acids to provide unique insights on a potential mechanistic link between altered intraluminal organic acids and fecal microbiota. DISCUSSION/SIGNIFICANCE OF IMPACT: Results may lead to development of targets for novel therapies and diagnostic biomarkers for IBS, emphasizing the role of the fecal metabolome.

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Primary management of advanced-stage ovarian cancer: 1 year at a high-volume care center

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OBJECTIVES/SPECIFIC AIMS: To describe the use of primary debulking surgery and neoadjuvant chemotherapy in advanced-stage ovarian cancer patients treated at Memorial Sloan Kettering Cancer Center (MSKCC) over the period of 1 year. Specifically, identify a subset of patients that are medically eligible to be considered for surgery. Examine the ultimate treatment designation for those patients, assessing the application of the MSKCC resectability algorithm and its utility in guiding treatment choice. METHODS/STUDY POPULATION: Using the prospectively maintained Ovarian Cancer Database at MSKCC, we queried patients who presented for initial management of ovarian cancer from July 1, 2015 to June 30, 2016. All patients with stage IIIB-IV disease who received their primary treatment at MSKCC were included in our study. Patients needed to have pathology-confirmed ovarian cancer and all histological subtypes were included. Data were collected and analyzed in Excel. RESULTS/ANTICIPATED RESULTS: There were a total of 173 patients treated for stage IIIB-IVB ovarian cancer at MSKCC during the study period. Of those 98 patients received PDS, whereas 75 were directed to NACT, making MSKCC's overall NACT rate

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43.4% for the year we studied. Of the patients who received NACT, 19 met full Aletti Criteria at diagnosis, precluding them from being considered for surgery. In addition, 21 patients had medical contraindications to surgery, meaning that a total of 40 patients who were given NACT were not able to be considered for PDS. If we then take into account only the patients who were medically eligible for PDS, the rate of NACT at MSKCC drops to 23.1%, almost half of the original value. These medically eligible patients are the population that should be receiving an MSKCC resectability score. Of the 98 patients who underwent PDS, 73.5% had a preoperative resectability score calculated. Based on the algorithm, 81.3% of those patients were deemed to be "low risk" and 15.2% were deemed to be "high risk" of a suboptimal debulking. The algorithm dictates that all "high risk" patients who go on to PDS should undergo a laparoscopy first to assess for resectability and potentially avoid an unnecessary open procedure. Hundered percent of the "high risk" cases that were taken to the OR had an initial laparoscopy before proceeding with PDS. Overall, 93.1% of patients that underwent PDS had an optimal cytoreduction, or ≤1 cm residual disease at the conclusion of surgery. Of the 6 patients throughout the year that had a suboptimal outcome, or >1 cm residual disease, 3 were initially scored as "low risk," 1 was scored as "high risk," and 2 did not receive an MSKCC resectability score prior to their procedure. Of note, 3 of the suboptimal cases had unresectable disease in an anatomical location not accounted for in the resectability algorithm. DISCUSSION/SIGNIFICANCE OF IMPACT: The rates of PDS Versus NACT vary widely between institutions, and it is not always clear how calculations are made. High-volume centers likely see a higher percentage of sicker patients with more advanced disease, which could increase their rates of NACT as many of these patients are not eligible for surgery. It is important to standardize the way our field quotes NACT rates, and to understand how treatment decisions are being made at a given institution. PDS has a demonstrated survival benefit, and while we would ideally use this modality for all of our patients, there will always be a baseline percentage of patients who cannot be considered for the surgery. Since we will never be able to offer those patients PDS, our objective should be to identify patients who can be considered for the procedure and to work toward optimizing their outcomes. In this study we identified the population of patients who are truly the PDS Versus NACT cohort as they were eligible for both modalities. We then examined the application and utility of the MSKCC resectability algorithm in an attempt to further optimize treatment allocation. This scoring system was implemented at our hospital over the past year with the goal that 100% patients going on to PDS would receive a preoperative score. Unfortunately, 26.5% of PDS patients were not scored prior to their procedure. This makes it more difficult to evaluate the efficacy of the scoring system, especially considering 1/3 of the suboptimal cases were not scored. Had these patients received a score, they might have been deemed "high risk" and could have avoided a lengthy operation with a significant chance of a suboptimal outcome. In addition, it is important to note that 3 of the suboptimal PDS outcomes were initially scored as "low risk," and 3 of the suboptimal outcomes were due to disease locations not accounted for in the original resectability algorithm. We will continue logging disease locations of suboptimal cases, it is possible that a certain disease location not in the scoring system is responsible for a significant portion of suboptimal outcomes. The resectability score model had an overall predictive accuracy of 0.756 when it was initially published, and we must continue tracking scores and outcomes to determine its validity when applied prospectively in our population. In order to accurately do so however, an emphasis should be made to ensure 100% of patients being considered for PDS receive a score going forward.

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Effects of a novel 2-phase rehabilitation program on postural control in older adults: A pilot study

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OBJECTIVES/SPECIFIC AIMS: Falls are a major source of morbidity and disability in the aging population. Twenty to thirty percent of older adults who fall suffer moderate to severe injuries such as lacerations, hip fractures, and head traumas. A serious component of falling often overlooked is the fear of falling. The fear of falling is part of a debilitating spiral that leads to decreased activity and muscle weakness. The goal of this investigation was to determine if a novel 2-phase rehabilitation program designed to reduce the fear of falling and increase muscle strength could improve postural control during falls in older adults with balance impairments. METHODS/STUDY POPULATION: Four older adults participated in 8 cognitive restructuring workshops entitled A Matter of Balance (AMOB): 2 hours/week, total of 16 hours, designed to restructure thought patterns relative to falls and reduce the fear of falling. Within 1–2 weeks of completion, participants enrolled in Phase II: a standardized 10-week lower-extremity strengthening program. Participants performed high-intensity concentric resistance exercise on a modified seated ergometer (Eccentron, BTE Technologies) twice per week for up to 20 minutes per session. Fear of falling was assessed using the Activities-Specific Balance Confidence (ABC) scale. Postural control was assessed during reproducible falls at 3 phases: baseline (T0), after Phase I AMOB (T1), and after Phase II strengthening (T2). Falls were induced by treadmill perturbations (VGait system, MotekForce Link) occurring at slow and fast belt accelerations. A 3 × 3 ANOVA was conducted on postural control outcomes with phase and stepping cycle as independent factors. Pairwise comparisons were analyzed with the Bonferroni correction. RESULTS/ANTICIPATED RESULTS: Statistically significant main effects were found for phase and stepping cycle ($p = 0.003$, $p = 0.00$). No statistically significant interaction effects were found. However, a trend toward increasing Center of Pressure-Center of Mass (COP-COM) distance occurred after each intervention phase (T1 and T2) during fast treadmill perturbations. The greatest increase in COP-COM distance was found at 100% of the stepping cycle during fast perturbations following 10 weeks of resistance training compared with baseline ($p = 0.006$). No significant differences were found in fear of falling between phases ($p = 0.682$). DISCUSSION/SIGNIFICANCE OF IMPACT: A large COP-COM distance suggests the individual is able to allow straying of the COM outside of the functional base while recovering balance. Meanwhile, a small COP-COM distance represents a conservative approach to postural tasks, in that the performer does not feel stable enough to allow separation of the COP and COM. These pilot data suggest that a 2-phase rehabilitation program can improve specific components of postural control during recovery from falls. Rehabilitation interventions aimed at reducing falls in older adults should consider adding a component of cognitive restructuring in conjunction with standard of care resistance training.

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Lower rates of influenza infection following 2 dose series of high-dose vaccination in plasma cell disorders: Results of a randomized, double-blind, placebo-controlled study

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OBJECTIVES/SPECIFIC AIMS: (1) Evaluate safety of a novel influenza vaccination strategy in patients with plasma cell disorders. (2) Measure laboratory-confirmed influenza infection rates following a novel influenza vaccination strategy in patients with plasma cell disorders. (3) Evaluate clinical correlates of response following a novel influenza vaccination strategy in patients with plasma cell disorders. METHODS/STUDY POPULATION: We conducted a double-blind, randomized study over the 2015–16 flu season, comparing 2 doses of Fluzone® High-Dose influenza vaccination (separated by 30 d) to the current standard of care influenza vaccination. Patients were allocated to the experimental arm in 2:1 ratio compared with standard of care arm. Standard of care influenza vaccination was considered single age-based vaccination (standard dose for those <65 y and high dosefor those ≥65 y) and patients in this arm received a saline placebo injection at 30 days to assist in blinding. Eligibility criteria allowed any patient with a PCD and no contra-indication to trivalent inactivated influenza vaccine. The primary endpoint was laboratory-confirmed flu infection rate. Protocol-driven surveillance screened patients for flu-like illnesses and performed laboratory testing for influenza until the end of the flu season in May 2016. Secondary endpoints include HAI titer serologic response rates, clinical correlates of protection from influenza infection, and exploratory studies of cell-mediated immunity through characterization of T cell subpopulations, cytokine profiles, and flu-specific T-cell responsiveness. RESULTS/ANTICIPATED RESULTS: In total, 122 plasma cell disorder patients were enrolled (97 with disease requiring therapy and 25 with asymptomatic gammopathy). Of those 48 patients received a single standard of care influenza vaccination and 74 patients received 2 doses of Fluzone® high-dose vaccine. Median age was 67 years (range 42–90). This 2-dose vaccination strategy was safely tolerated in all patients with no grade 2 adverse events attributed to vaccine. With close clinical follow-up, only 4% of patients receiving 2 vaccine doses developed laboratory confirmed influenza Versus 8.3% of those receiving single vaccine. When compared to the expected CDC influenza infection rate of 10%–15%, 1 sample, 2-tailed binomial testing revealed patients receiving 2 vaccines experienced a significantly lower rate of infection than the expected rate ($p < 0.05$) whereas those receiving single vaccine showed no significant difference ($p = 0.38$). DISCUSSION/SIGNIFICANCE OF IMPACT: This randomized study demonstrates that the 2 dose strategy of Fluzone® high-dose influenza vaccine is safely tolerated in patients with plasma cell disorders and associated with significantly less than expected laboratory-confirmed influenza infections. The results suggest that this novel

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