PRIMARY RESEARCH

Phase II Clinical Drug Trial to Assess the Safety and Feasibility of High Dose Vitamin D3 in Pediatric Patients with Cystic Fibrosis

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Background: Children with Cystic fibrosis (CF), due to intestinal malabsorption and pancreatic insufficiency, are at risk of developing a vitamin D (vit D) insufficiency. In this population, vit D insufficiency has been linked to increased inflammatory markers, poor bone health, and increased frequency of lung infections. Treatment guidelines (to correct a vit D insufficiency in CF) were published by the CF Foundation in 2012. Since that time, our clinic has continued to observe poor vit D levels despite additional supplementation per these guidelines.

Research Objectives: To assess if a single oral high dose (250,000 International Units (IU)) of vit D3 is safe and feasible.

Methods: This study is a one-arm phase II clinical drug trial in pediatric patients with CF aged 3 to 18 years followed in the John's Hopkins All Children's Pediatric CF center. Inclusion criteria was met by patients with 25OHD <30 ng/mL (vit D insufficiency). Exclusion criteria included any history of kidney disease/stones, hypercalcemia/hypercalciuria, abnormal creatinine levels 2 times the upper limit of normal (ULN), CF liver disease/cirrhosis, elevated liver transaminases 5 times ULN, parathyroid disorder or pregnancy. Subjects were provided a single dose during CF clinic. Safety was assessed with a serum calcium (Ca) level and a serum phosphorus (Phos) level measured at 1 week and 3 months following the dosage based on the half-life of vit D and based on CF standard treatment guidelines. If Ca or Phos were elevated, a parathyroid hormone level (PTH) and spot urine Ca to creatinine ratio was obtained. To assess feasibility, participants answered a 10-item questionnaire on gastrointestinal symptoms experienced and overall ease of the regimen. Based on power analysis using another similar study, a total of 27 patients were enrolled.

Results: Only three patients had safety labs that required additional investigation. All levels resolved without additional treatment and were not clinically significant or harmful to any of the patients. One patient had hypercalcemia and three patients had hyperphosphatemia where two patients in total required PTH levels. The feasibility questionnaire indicated that this regimen was feasible as all 27 participants indicated that they preferred taking a one-time high dose over daily vitamin D and indicated that they would do this regimen again. Additionally, only 5 participants reported complaints of stomach upset after treatment, but this subsided shortly after. Although statistical analysis is still being completed, at baseline, mean vit D levels were at 22.7 ng/mL and went up to a mean level of 29.1 ng/mL at 3 months. It is also unclear at this time if this increase in vit D levels from baseline to 3 months is significant.

Conclusion: Based on these findings, where none of the participants required treatment for hypercalcemia or hyperphosphatemia, oral, high-dose vit D3 can be safely administered to pediatric patients with CF. This regimen may also be a feasible option for pediatric patients with CF, based on the feasibility questionnaire.

Primary Research on Low-cost Microbial Testing of Botanicals for Small Herbal Businesses

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Background: Small herbal businesses face costly challenges to comply with FDA's Good Manufacturing Practices (GMPs). Current testing for microbial contaminants occurs in microbiological laboratories - a significant expense. An alternative methodology that requires minimal training and equipment to test for microbial contamination of herbal products would reduce financial burden, increase compliance, and improve the quality and safety of herbal supplements. Methods and training were developed to establish workspaces necessary to meet ISO environmental bioburden standards recommended in microbiological labs using aseptic techniques and Biosafety Level 1 (BSL-1) requirements, with appropriate positive/negative controls for environmental monitoring.

Research Objectives: This study aims to 1) characterize whether training of aseptic techniques in a BSL-1 environment and use of 3M™ Petrifilm™ methodology for the Microbiological Examination Testing (MET) can replicate microbiological laboratory conditions necessary to test microbial load in herbal supplements and 2) assess variability of microbial growth for multiple herbal formats.

Methods: Pilot testing conducted at JIFSAN laboratory (control) was compared to identical samples tested in non-laboratory workspaces. *Echinacea* tinctures at 45%, 60%, and 95% alcoholic strengths were tested in triplicate with negative controls using 3M™ Petrifilm™ for aerobic count (AC), yeast/mold (YM), and *E.coli*/coliform (EC) at five workspaces. The range of tinctures was selected to test the bactericidal activity of ethanol on microbial load.

The methodology was expanded to test multiple *Echinacea* formats for compliance with USP recommended microbial limits for botanicals. Concurrently, methods and training were assessed using three participants at MUIH Dispensary to gauge operator variability. Samples were prepared to establish dilution parameters for crude herb and decoction, then tested once per dilution/operator for AC, YM, and EC with negative controls. Positive controls (active bacteria) were not introduced.

Results: A consistent pattern of growth appeared based on the level of alcohol in the comparison study with JIFSAN for all 3 tinctures (45%, 60%, and 95%) tested. All results were 0.0 cfu except the 45% tincture for AC: AVG 96.66 cfu, STD = 106.48. This is comparable to the JIFSAN control: AVG 83.33 cfu, STD = 116.90. Methods and training appeared to be effective in the format analysis: all formats met USP standards.

Conclusion: The development of a microbial testing method, requiring minimal training and low-cost equipment, performed in non-laboratory settings has potential replication by small herbal businesses for cGMP compliance. Larger sample size data would strengthen the statistical basis to develop a validated method for use by industry.

The Use of Acupressure to Decrease Anxiety in Hospitalized Orthopedic Trauma Patients Requiring Surgical Intervention: A Mixed - Methods Study

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Background: Acute Stress Disorder (ASD) describes the acute stress phase following exposure to a traumatic event. One specific population at risk for ASD is hospitalized orthopedic trauma patients. Presently, treatment of ASD and its sequelae, such as anxiety, is limited to conventional methods such as cognitive behavioral therapy (CBT) and pharmacologic management. The use of complementary and integrative health (CIH) practices to manage health care outcomes, such as anxiety, is on the rise. CIH therapies have been studied for their safety, efficacy and cost efficiency in anxiety reduction and may have a place in the treatment of ASD.

Research Objectives: Acupressure, a type of CIH therapy, uses manual finger pressure on accepted acupoints throughout the body. It is considered a form of acupuncture and is hypothesized to release neurotransmitters that contribute to relaxation. It has been previously demonstrated to have no serious adverse effects. The SEVA acupressure protocol was developed to elucidate a relaxation response in patients experiencing stress/anxiety. The goal of this study is to determine the utility of the SEVA protocol in reducing anxiety in the specific patient population of orthopedic trauma patients.

Methods: A convenience sample of 14 patients from an orthopedic trauma center was screened and recruited into the study. Using a mixed methods approach, the Visual Analog Scale-Anxiety (VAS-A), a 100-mm scale was used to measure anxiety scores before and after the SEVA protocol was administered and; descriptive phenomenology was used to describe the patient's experiences with acupressure from a semi-structured interview.

Results: There was significant effect for time after the SEVA protocol was administered, $F(2,12) = 11.85$, $p < .001$, with the average anxiety score pre-intervention measured at 66.1, the average post-intervention score at 28.6 and the 15 minute average post-intervention score at 27.8. Additionally, qualitative results reflected themes of impact on physiologic response, expectations of the session and perception of the session.

Conclusion: Acupressure is an inexpensive, non-invasive treatment modality for management of anxiety in the hospitalized orthopedic trauma patient population. The protocol used in this study is easy to teach and learn and staff and family members can use these points to reduce anxiety, both in the hospital and beyond, making non-pharmacologic healing a real possibility.

A Mixed-Methods Assessment of Clinical Judgement, Critical Thinking Skills, and Applications Among Integrative Dietitian Nutritionists

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Background: Integrative and functional nutrition (IFN) is an area of nutrition and dietetics practice where critical thinking skills and processes of registered dietician nutritionists (RDNs) are especially important. In clinical practice, it is important to achieve and maintain consistency in providing care, utilizing evidence-based guidelines when available. Limited evidence-based practice guidelines exist for IFN RDNs, thus individual practitioners must use critical thinking skills to appraise the scientific literature.

Research Objectives: The purpose of this mixed-methods study was to describe the critical thinking skills and processes IFM RDNs use in providing patient care, using in-depth interviews and validated assessment tools.

Methods: Purposeful sampling identified practicing IFN RDNs, proficient or higher in IFN dietetics-based eligibility criteria adapted from the Commission on Dietetic Registration's specialty and advanced level credentials. Strict inclusion criteria were developed to ensure potential participants met knowledge, experience, and expertise. Potential participants list was developed by: RDNs currently practicing at US centers providing IFN services, asking study participants for referrals and through a DIFM e-mail to eligible members. Participants (n=16) thought aloud during a case study. Content analysis was conducted to identify NCPM domains and concepts within the case study. Transcripts were coded based on nutrition standardized language. RDNs (n=19) completed the Health Sciences Reasoning Test with Numeracy (HSRT-N) and the California Critical Thinking Disposition Inventory (CCTDI).

Results: Sixteen participants completed the case study. Nineteen participants completed the critical thinking assessments. The most frequent code was "Assessment Critical Thinking Skills" (i.e. obtain more information) applied 249 times (27.8% segments). The most frequently used code was Food/Nutrition-Related History (Assessment). The mean score on the HSRT-N was 81.6±7.0 (max = 100), with highest scale scores on Induction, Explanation, and Analysis. On the CCTDI, medical center RDNs scored significantly higher in Inquisitiveness than private practice RDNs (52.1±4.0 vs 47.3±4.2 p=0.025)

Conclusion: Experienced IFN RDN participants possessed a high degree of critical thinking skills, measured by validated quantitative tools and used them in addressing a patient case study. Those in interdisciplinary environments were more inquisitive than sole practitioners. The working environment may have an impact on their willingness or ability to obtain new information or seek out explanations.