Title Effect of Vitamin D Supplementation on Balance in CKD

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METHODS

A sample size of 30 patients with ESRD5D (ages 21-70 years) will be utilized for this study. The thirty subjects will be randomized to intervention or active control; 15 per group. We anticipate a 20% drop out rate and an additional 10% screen failure rate. Therefore, we anticipate consenting a total of 40 subjects. Subjects will be recruited through Nebraska Medicine Nephrology clinics.

Subjects will be consented and screened in the Diabetes Center at UNMC. All candidates for the study will be adults (aged 21-70 years) on maintenance hemodialysis at any UNMC directed dialysis unit. Other inclusion criteria include 1) a timed up and go score of > 13.5 seconds;[19] 2) ambulatory, without a walking aid (i.e., cane or walker); 3) able to complete the various questionnaires interactively with the research nurse; 4) venous access that can be accomplished without unusual difficulty; and 5) greater than 3 months on hemodialysis. Subjects will be excluded if they are 1) pregnant; 2) on peritoneal dialysis; 3) allergic to vitamin D; 4) have diagnosed liver disease; and/or 5) an intestinal disorder that would interfere with vitamin D absorption. They will also be excluded if they are currently taking vitamin D supplements >800 IU per day, glucocorticoids, anticonvulsants, or other drug therapies for osteoporosis.

At the baseline visit, the subject will be screened for eligibility by a physical exam, including vital signs, height, weight, and a detailed history, including medical history, medications, personal fracture & fall history, menstrual history, diabetic history, sun exposure history, and alcohol and tobacco use. Vital signs, height, and weight will be recorded. A validated Food Frequency Questionnaire will be completed to assess dietary vitamin D intake. Previous records of health history and fracture documentation will be requested. Each subject will undergo phlebotomy of 13ml.

Subjects will be randomized into one of two groups. Each subject will take a daily, oral capsule containing vitamin D (4000 IU) for 3 months or active control (800 IU vitamin D). We chose to use a daily dose, as it has been proposed that a steady state of vitamin D levels provides a constant source of substrate for enzymes converting it to 25(OH)D.[20] This dose will increase serum 25(OH)D levels to ~60 ng/ml by 12 weeks. The active control will be 800 IU of vitamin D consistent with the recommendations developed by the Food and Nutrition Board of the Institute of Medicine.

Subjects will then travel to the Biomechanics Research Building at the University of Nebraska at Omaha. Subjects will then be asked to undergo static and dynamic balance tests, the timed up and go (TUG), the Fullerton Advanced Balance scale (FAB), and gait speed over 20 meters (see Functional test descriptions below). They will also undergo muscle strength and endurance testing of the quadriceps and hamstrings of both limbs. The subject will be issued a pill bottle containing a 3-month supply of the interventional drug (see below). A fall diary will be given to the subject as well.

At 3 months of the study, the subject will be interviewed for changes to medical history & sun exposure. Height and weight will be recorded. Subjects be asked to undergo the same physical function tests as baseline. Each subject will undergo phlebotomy of 13ml. Pill bottles will be collected for a pill count.

Functional test descriptions:

Static and Dynamic Balance: will be measured through the Neurocom Balance Manager System. The two laboratory tests that will be used are the Sensory Organization Test (SOT) and the Motor Control Test (MCT). The purpose of the SOT is to assess the three sensory systems that encompass balance. There are six conditions (combinations of manipulating vision,

proprioception, and the vestibular system) with 3-20 second trials for each. The SOT provides an equilibrium score that is ranked on a 0-100% scale, where 0%=reaching the point of falling or has fallen and 100%=no movement of the body while standing. The purpose of the MCT is to examine the body's automatic response to correction of posture to a moving surface. There are three trials and six conditions in which the base that the subject stands on is perturbed slightly (moved forward or backward). The MCT scores for latency, the time it takes in milliseconds (msec) for an individual's center of gravity to respond to the movement. A longer latency would indicate that it takes longer for the nervous system to respond to the movement.

Timed Up and Go (TUG): The subject is observed while rising from a chair, walking 3 meters, and returning to the chair. A score >12 seconds is indicative of fall risk.

Fullerton Advanced Balance scale (FAB): is a series of balance tests to assess the subject's ability to use his/her somatosensory cues to maintain upright balance in varying situations. There are ten tasks in the scale and they are scored on a range from zero to four. Zero being unable to complete the task and four being able to complete the task independently with no assistance. Scoring less than 25/40 is considered to be at risk for falling.

20-meter Gait Speed: provides a marker of health status and survival.21 The subject will be instructed to walk 20 meters at his/her preferred walking speed. Time is measured while the individual walks the set distance.

Muscle Strength and Endurance: Quadriceps and hamstring muscle strength and endurance will be assessed using an isokinetic dynamomenter (Biodex System 4, Biodex Medical Systems, Inc., Shirley, NY). Both limbs will be assessed. Standard testing protocols will be used. This testing will be done at the end of the visit as other measures could be affected by the fatigue induced by this testing.

Dependent variables will be checked for normality. Non-parametric tests will be utilized where appropriate. For each outcome, linear mixed-effects models (LMM) will be conducted. The model will include one of the dependent variables as the outcome variable and treatment group and time as independent variables as well as their interaction. The LMMs will also be adjusted for possible covariates (e.g., age, medication history, sun exposure). Significance will be determined at an alpha < 0.05 level.

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