Nutrition Epidemiology Study Proposal:

Supplemental Vitamin D and Physical Performance Amongst Elderly

The benefits of vitamin D relating to bone health are well-known. Detection of vitamin D receptors in muscle tissue of humans has led researchers to formulate new hypotheses concerning an association between vitamin D and muscle health (1). The role of vitamin D in muscle maintenance has been investigated among the elderly: a population that experiences age-related sarcopenia and subsequent decline in physical performance (2). This population has been well-documented as having chronically low levels of vitamin D, as evidenced by biomarker serum 25-hydroxyvitamin D (25-OHD). Various factors contribute to vitamin D insufficiency and deficiency in the elderly, including low dietary intakes and reduced sun exposure in conjunction with a diminished ability to synthesize vitamin D (2). Vitamin D deficiency is a major public health concern amongst the elderly as deficiency has serious health implications; Osteomalacia is of special concern due to its characterized symptoms of muscle pain and proximal muscle weakness (2). Such weakness contributes to issues with balance and gait that lead to falls. Falling is associated with physical decline and hip fractures are common (1). Though the role of vitamin D in musculoskeletal strength has yet to be determined, ongoing research aims to investigate the hypothesis that increasing serum vitamin D will increase muscle strength of the lower extremity.

Limitations of Existing Literature

Moreira-Pfrimer and Pedrosa et al. conducted a randomized double-blind controlled trial that examined the effects of vitamin D supplementation on institutionalized elderly (3). After a

6-month period, vitamin D in the form of cholecalciferol (D3) was found to increase lower extremity strength, independent of physical activity (3). This study is noteworthy for 2 reasons: the study population was institutionalized, and improvements were observed despite any change in physical activity. Physical activity is thought to play an important role in bone health in order to increase bone mineral density; in this study, absence of activity outside of everyday living emphasizes the effectiveness of supplementation on the elderly population. In addition, institutionalized elderly are known to be exceptionally weak. The fact that benefits were evident not only in the absence of physical activity, but also among the weakest population, demonstrates apparent usefulness of supplementation.

It should be noted that supplemental vitamin D was administered in combination with calcium (3). Calcium plays a pivotal role in the prevention of osteoporosis; absorption of calcium is dependent on adequate quantities of vitamin D (4). Vitamin D allows the formation of calcitriol; hence, these nutrients are often administered together to promote the formation of new bone and prevent deterioration of existing bone (4). Despite the optimistic findings of Moreira-Pfrimer and Pedrosa et al., the inclusion of calcium is a limitation if results are to be formed on the basis of isolated supplemental vitamin D. Because calcium and vitamin D work in conjunction, it is impossible to determine if these nutrients would be as effective if administered independently.

The same limitation exists in research conducted by Bischoff and colleagues. Calcium was included in both treatment groups in a randomized controlled trial investigating falls among a population of elderly women (1). Though the presence of vitamin D decreased fall risk by 49 percent compared to calcium treatment alone, the treatment of vitamin D was administered along

with 1200 mg calcium. Therefore, it is unclear if fall risk would have decreased by the same percentage had calcium been omitted from treatment.

Manoy and Yuktanandana et al. examined the effects of vitamin D supplementation alone on (knee) osteoarthritis patients (5). The study took place over 6 months and all participants received 40,000 IU vitamin D. Findings included a reported improvement in both physical performance and quality of life (5). Quality of life improvements were indicated by analog scales of perception and pain; physical performance encompassed 4 separate tests as well as grip and knee extension force measurements. This study also took several biochemical factors into consideration.

Despite promising conclusions that vitamin D supplementation is beneficial to overall quality of life and physical performance, the results cannot be generalized to the elderly. A limitation is the form of vitamin D administered. This study took place in Thailand, where vitamin D3 is not recognized as a "first-line drug…in the hospitals and public health sectors" (5). Vitamin D2 (ergocalciferol) was therefore used as the only treatment method. Due to differences in potency and metabolism between plant and animal forms, it is unclear if vitamin D2 would be an effective treatment when used in elderly patients. Another limitation was lack of control group. Consequently, patients were not blinded; placebo effect may have played a role in reported improvements.

Finally, there are general limitations of the aforementioned studies. Current studies include more women than men due to life expectancy trends. When studying the elderly, high drop-out rates are common as a result of deteriorating health status, transfer between geriatric centers, and death. Thus, small sample sizes are to be expected when investigating elderly

populations. In addition, seasonal variations must be considered as well as geographical location as summer seasons and warmer climates may influence the severity of deficiency.

Hypothesis: Supplemental cholecalciferol (vitamin D3) will increase musculoskeletal performance (compared to baseline) among elderly, independent of calcium.

Proposed Study Design

The study design will utilize a clinical trial methodology. There will be 2 groups, both will receive treatment over a 6-month period. The first group will receive supplemental vitamin D3 as 800 IU per day. The second group will receive 800 IU per day in combination with 1200 mg of Calcium, divided into 2 doses to maximize absorption. These dosages were selected based on existing literature as well as recommendations discussed by the National Institutes of Health, suggested for individuals who are 70 years of age (4).

Baseline testing will include verified measures of physical performance. These measures include: grip strength, assessed by grip strength dynamometer; and sit-to-stand tests (STS), assessed by recording the duration of time (in seconds) required by subjects to execute 5 chair stands without the aid of the upper extremities. Baseline serum measures of 25-OHD, Calcium, and iPTH will be taken; subjects will be matched for level of insufficiency/deficiency, age, gender, and race/ethnicity. Physical performance and serum measures will be taken at baseline, 3 months, and 6 months to monitor treatment.

Strengths of the proposed design include supplementation of vitamin D in D3 form, which has shown to be more bioactive compared to the D2 form (6). Collecting serum values of 25-OHD, Calcium, and iPTH will provide greater insight into subject biochemistry; specifically, bone metabolism. Repeating tests of physical performance and serum biomarkers 3 times

throughout the course of the study will enhance evaluation of the treatment. The most notable strength that addresses weaknesses of earlier studies is having 2 separate treatments. By administering supplemental vitamin D independent of calcium, the study design will allow researchers to examine the effectiveness of vitamin D alone. Likewise, the added benefits of calcium can be gauged by comparing serum levels and performance scores across groups.

Limitations involve measuring complex physiological processes. Severity of deficiencies may influence outcomes, but subjects will be matched as closely as possible based on baseline levels and indications of bone health status. Age and gender may be a concern; as mentioned, women tend to outnumber their male counterparts. Additionally, 6 months is a considerable amount of time to study a population that is known to have high drop-out rates. The design also lacks a control; placebo effect could influence performance scores. Finally, seasonal variations may impact serum levels of 25-OHD. This presents a number of confounders, including sun exposure, skin pigmentation, use of sunscreen, and individual abilities to synthesize vitamin D.

A large population size would be preferred, but considering the limited subject availability among the age group of interest, a smaller sample of approximately 100 people will suffice. Recruitment would take place at a local nursing home, where subjects will be approached by staff to participate. During the study period, nurses will administer treatment in capsule form at scheduled breakfast and dinnertimes. Subjects will be supervised to ensure successful administration.

Dietary intake will be evaluated by trained dietetic interns, who will record the weight of foods at the start of meals and the weight of any foods that remain uneaten. Common food items of the nursing home will be included in a database to measure nutrient intakes. This is a strong methodology as it eliminates reliance on memory among a population that may have difficulty

recalling meals. Limitations include dependency on dietetic interns to accurately assess foods eaten.

Results of baseline, 3-month, and 6-month testing will be documented. Typical dietary intakes will be measured using the previously mentioned database. As discussed, participants will be matched for level of vitamin D and Calcium insufficiency/deficiency at baseline, gender, and race/ethnicity. Baseline test results will be compared to test results obtained at 3 months and 6 months. Changes in biomarkers and performance scores will be compared across treatment groups.

Results of the proposed clinical trial will be employed by researchers to draw conclusions about the effectiveness of vitamin D3 supplementation on physical performance among an elderly population. Literature of existing studies has not investigated the role of vitamin D3 in the absence of calcium in older persons. Data relating to serum level changes in response to treatment as well as changes in physical performance will increase understanding of the effects of supplemental vitamin D3 and physical performance amongst elderly. Preexisting hypothesized benefits of combining supplemental vitamin D with Calcium to improve subject outcomes will be examined. This objective is measurable due to the inclusion and comparison of 2 treatment groups.

Generally speaking, results of the proposed investigation will contribute to existing knowledge of the topic at hand. This study design is unique in that it examines the impact of supplemental cholecalciferol, both independently and in conjunction with supplemental Calcium. Research conclusions can be referenced by healthcare professionals and Registered Dietitians to improve outcomes of older persons as it relates to musculoskeletal health via dietary supplementation.

References

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