Title: Effect of Soluble Corn Fiber Supplementation for 1 Year on Bone Metabolism in Adolescents

NCT Number: NCT02916862

Date of the document: 09/26/2025

STUDY DESIGN AND METHODS

Study rationale and overall design

The MetA-Bone trial was a double-blinded placebo controlled clinical trial to determine the effects of SCF supplementation for one year on bone mass in children and adolescents. Details of the trial were published elsewhere (25). Briefly, the primary outcome was change in total and spine BMC between baseline and 6 months and between baseline and 12 months. The Institutional Review Board at Florida International University (FIU) approved the study. Also, a Data and Safety Monitoring Board (DSMB) was established and approved by NIH, with yearly meetings to assess safety reports.

Study population

Healthy children and adolescents aged 9-14 years were recruited in the Miami Metropolitan Area. Participants were recruited from various sources from X to X, as previously described (26). We aimed to recruit children and adolescents at a pubertal development (based on Tanner stage) of 2-4 to match the previous study on SCF supplementation for three-week in adolescents conducted by Dr. Weaver (12). We also aimed to include only those children consuming 2 or fewer servings of dairy products per day, which translates into about 600 mg/d of calcium (half of the recommendation for this age group (27)) and consuming calcium supplements <200 mg/d. Participants were excluded if they had a body mass index (BMI) percentile above 95% for age and sex based on the Centers for Disease Control Growth Charts, any chronic illness requiring regular medication, or vitamin D deficiency (25OHD <20 ng/ml), as established by the Institute of Medicine for bone health (28). This criterion was assessed at the baseline visit. After finding many children with low vitamin D in the baseline visit (29), the protocol was amended to provide vitamin D supplements to those children for 6-8 weeks and once 25(OH)D was >20 ng/ml, they were randomized into the study.

Supplements

Participants were randomized sequentially using a computer-generated block randomization list into four groups: SCF (12 g/d), SCF + calcium (12 g/d of SCF + 600 mg/d of elemental calcium), Placebo (12 g/d of maltodextrin); or Placebo + calcium (12 g/d of maltodextrin + 600 mg/d of elemental calcium). SCF and the maltodextrin were donated in part by Tate & Lyle PLC (Hoffman Estates, IL) and the calcium (in the form of calcium lactate gluconate) was purchased from Stauber

Fullerton, CA. Supplements were pre-mixed in our diet preparation lab at FIU by a dedicated research team not involved in the assessments and delivered to participants in large white canisters of the same size and weight with a color-coded lid for a 3-month supply. Participants were instructed to consume 1 scoop of product diluted in 8-10 ounces of liquid twice per day. The study supplements were tested several times per year for microbiology integrity (aerobic plate count, coliforms, E. coli, Salmonella, yeast, and mold) by an independent external laboratory.

To promote retention, participants were given the choice of either adding the supplement to their usual beverage (non-carbonated) or to be pre-mixed in our food lab with Kool-Aid (donated by Kraft). Several flavors were offered, and they could change the flavor every 3 months. We also provided a study water bottle to facilitate taking it to school, travel, or extracurricular activities. We also sent motivational text messages about the importance of taking the supplement, how to establish the habit of taking it daily, and ideas to vary the supplement using an automated one-way text message provider. The text messages were sent twice per week for the first 6 weeks and then the frequency was reduced to every 3 weeks until the end of the study. We provided enough supplement in each canister to share with family members.

Compliance was carefully monitored during the trial and recorded in different ways. We initially developed an app to record compliance daily, but after discussing with parents their use, this was changed to a weekly survey sent by text. We also provided a paper calendar as an alternative. We asked families to record the number of supplements consumed per day (2, 1, or 0). Parents received extra compensation for monitoring supplement intake every 3 months. In addition, they were asked to complete a short questionnaire about the study supplement intake at every visit (3, 6, 9 and 12 months). Lastly, we reviewed compliance at every visit verbally. There was a dedicated person compiling the various sources of compliance information to identify when data was missing and if we needed to contact parents to discuss low compliance.

Measurements

As previously described (25), the research team was blinded to the supplement type. Participants were asked to complete three visits (baseline, 6 months, and 12 months) at our FIU labs to undergo anthropometrics and a bone scan, and complete health questionnaires. Also, participants were asked to provide a fasting blood sample, a 24-h urine collection, and a fecal sample at baseline and

12 months. We also visited participants at their home or other convenient place for the 3- and 9-months visits to deliver more supplements and complete health questionnaires.

General health and socio-demographics: this included parental age, sex, education, and medical history and children's age, sex, self-reported pubertal maturity using Tanner staging (30) and menarche date (if applicable), fracture(s) history, use of medications, use of alcohol and tobacco, sleep and stress.

Anthropometric measurements: weight, height, and waist circumferences were assessed by trained study staff at baseline, 6-month and 12-month following standardized protocols. Weight velocity and height velocity were calculated as the difference in weight or height, divided by the difference in age between consecutive annual study visits. Height velocity <0 cm/year was assumed to reflect a measurement error after reaching adult height and was recoded to 0.

Bone mass: Whole body and spine BMC and BMD were assessed using a Hologic dual-energy X-ray absorptiometry (DXA) scan at our FIU DXA Lab at baseline, 6-month and 12-month following standardized protocols. All scans were performed by trained personnel, with the Florida Department of Health Certification for Basic X-ray machine operator.

Blood sample: a fasting blood sample (15 ml each) was collected at baseline and 12-months by venipuncture by research trained phlebotomists. Samples were immediately centrifuged; part was sent to a commercial lab for 25(OH)D, calcium, phosphorus, and creatinine. The rest was stored at -80°C for future analyses.

Urine sample: a 24-h urine sample was collected at baseline and 12-months and analyzed by a commercial lab for calcium, phosphorus, and creatinine.

Diet: Three 24-h recalls were collected at baseline, and a 24-h recall was collected at 3, 6, 9, and 12 months. Dietary recalls were analyzed using the Nutrition Data System for Research (NDSR) software. Total energy intake and intakes of protein, calcium, vitamin D were calculated to be used as covariates in the statistical analyses.

Physical activity: This was collected at each visit using the International Physical Activity Questionnaire (IPAQ) (31) and used as a covariate in the statistical analyses.

Gastrointestinal symptoms: This was recorded every 3 months with a survey asking participants for abdominal pain, bloating, flatulence or diarrhea.

Statistical plan

Sample size was calculated for the primary outcome (change in whole-body BMC over 1 year between SFC and control) based on a conservative clinically meaningful standardized effect size (32), as when the study started, there were no previous studies assessing the effects of SCF on bone. For an alpha level of 0.05, 40 in each group provides 80% power to detect a medium effect size of 0.5 units of standard deviation (33) in BMC between any of the active treatment groups compared to placebo. This was inflated by >30% for non-eligible rate due to vitamin D deficiency (10%) plus drop-out rate similar to rates in our previous trials among adolescents (20%) (34–38). All power calculations were performed with PASS2019 (39).

The main analyses will be performed on an intention-to-treat basis. Data was examined for outliers and normality. Descriptive statistics included means, medians, standard deviations, and ranges for continuous variables and frequencies and proportions for categorical variables. ANOVA and chi-square test were used to compare means and proportions by treatment group. We used the same analytical methods to examine potential differential attrition by treatment group. We compared characteristics and determined missing data mechanism between study completers and those with missing outcome data, using two-sample t-test for continuous and chi-square test for categorical variables. For the primary analysis, percent change from baseline in whole-body BMC after one year of supplement was compared between the two groups using analysis of covariance, adjusted for baseline age, sex, Tanner stage (puberty status), weight velocity and height velocity. Data was analyzed using SPSS. Effects were considered significant at the alpha level of 0.05.