Diabetes Mellitus and Glucose Metabolism

CLINICAL STUDIES IN OBESITY, DIABETES RISK, AND CARDIOVASCULAR OUTCOMES

Dietary Reduction of Branched-Chain Amino Acids

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Background: One of the primary risk factors for the development of diabetes is obesity. Although moderate weight loss can lead to improvements in metabolic health, reduced-calorie diets are difficult to sustain. A number of groups have shown that low protein diets are associated with metabolic health in both rodents and humans. In particular, the branched-chain amino acids (BCAAs) leucine, isoleucine, and valine are associated with insulin resistance and diabetes in humans. Blood levels of the BCAAs decrease in humans fed a low protein diet, and we recently showed that reducing either dietary BCAAs or protein rapidly restored normal body composition and insulin sensitivity to diet-induced obese mice without reducing calorie intake. We are determining the effect of a low BCAA diet in humans with prediabetes and overweight/obesity.

Objectives: The primary outcome is the reduction of dietary BCAA intake by at least 50% in subjects in the low BCAA group while maintaining overall baseline calories. Secondary outcomes are compliance and tolerability of the low BCAA protein powder.

Method: This is a randomized, controlled, single-blind pilot study. The intervention arm uses a low BCAA protein powder to replace two meals per day for 60 days. The control arm uses a control protein powder with standard amounts of amino acids to replace two meals per day for 60 days. We are enrolling 16 males with the following criteria: ages 35 to 65, BMI 28 to 35, and hemoglobin A1c 5.7%-6.4% or fasting glucose 101-125 mg/dL. A registered dietitian reviews a 4-day food diary prior to diet initiation and creates an individualized meal plan based on those values in order to maintain baseline calories during the study diet. Baseline measurements prior to diet initiation include waist circumference, body mass index, fasting insulin and glucose, an oral glucose tolerance test, resting metabolic rate, body composition testing using dual energy x-ray absorptiometry, jumping mechanography to assess muscle function, and a stool sample to assess the microbiome. These tests are repeated after 60 days on the diet. Safety labs are performed while on the diet and 2-3 weeks after the end of the diet. Weekly safety telephone calls occur while on the diet. The food diaries are repeated after 30 and 60 days on the diet.

Results/Conclusion: Ten of sixteen subjects have completed the trial to date. One out of four subjects in the low BCAA group dropped out; the remainder successfully completed the study. BCAA intake was successfully reduced by 50%. Missed beverages were uncommon. No significant safety concerns or side effects have been noted. In conclusion, our early results suggest that replacement of two meals a day with a protein powder lacking BCAA for up to two months is a safe and feasible intervention. Ongoing analysis will determine if this intervention impacts metabolic health.

Bone and Mineral Metabolism

OSTEOPOROSIS AND VITAMIN D

Comparison of Vitamin D Metabolism in Deficient and Sufficient States

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Objective: to study the differences in calcium-phosphorus and vitamin D metabolism in healthy individuals with deficient and sufficient baseline state of vitamin D. Materials and methods: The study included 16 young conditionally healthy individuals, divided into two equal groups: with levels of 25(OH)D below and above 30 ng/ml determined by the immunochemiluminescent method (Group A and Group B respectively; DEQAS certified). All participants were evaluated for the biochemical parameters of blood and urine, characterizing calcium-phosphorus metabolism, PTH by commercial methods, and vitamin D metabolites (25(OH)D3, 25(OH)D2, 3-epi-25(OH)D3 and 24,25(OH)2D3) by HPLC/MS-MS before oral intake of 150 000 IU of an aqueous solution of cholecalciferol and 7 days after administration. Results: At baseline, the level of vitamin D metabolite 25(OH)D2 in Group B was lower with no significant differences in other studied parameters. In group A, strong positive correlations were observed between levels 25(OH)D3 and 3-epi-25(OH)D3, 24,25(OH)2D3, while in group B there were no such associations. After taking a loading dose of cholecalciferol, the groups showed generally similar changes in the studied vitamin D metabolites: a statistically significant increase in 25(OH)D3, 3-epi-25(OH)D3, a decrease in 25(OH)D2, and a ratio of 24,25(OH)2D3 to 25(OH)D3. However, the level of 24,25(OH)2D3 did not change in group B, with a significant increase in group A. The medians of the studied biochemical parameters in blood/urine, as well as PTH, remained unchanged in both groups. Conclusion: In patients with inadequate baseline levels of 25(OH)D, after a loading dose of cholecalciferol, there is a tendency to formation of more inactive forms of vitamin D. These deviations in the metabolism of vitamin D need to be clarified, since they can potentially affect the effectiveness of cholecalciferol therapy.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Analysis of Adverse Events in Adult Patients with Acromegaly Receiving Oral Octreotide Capsules: Results from the Phase 3, Randomized, Double-Blind, Placebo-Controlled CHIASMA OPTIMAL Study

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