Abstract


Calcium and 1,25-dihydroxyvitamin D3 modulate genes of immune and inflammatory pathways in the human colon: a human crossover trial.


Yale University and Veterans Affairs Connecticut Healthcare System, New Haven, CT; The Rockefeller University, New York, NY; The Rockefeller University, New York, NY; Albert Einstein College of Medicine, Bronx, NY; and Weill Cornell Medical College, New York, NY.

BACKGROUND: A high dietary calcium intake with adequate vitamin D status has been linked to lower colorectal cancer risk, but the mechanisms of these effects are poorly understood.

OBJECTIVE: The objective of this study was to elucidate the effects of a Western-style diet (WD) and supplemental calcium and/or 1,25-dihydroxyvitamin D3 [1,25(OH)2D3] on the colorectal mucosa.

DESIGN: We conducted 2 crossover trials to define molecular pathways in the human colorectum altered by 1) a 4-wk WD supplemented with and without 2 g calcium carbonate/d and 2) a 4-wk WD supplemented with 1,25(OH)2D3 (0.5 μg/d) with or without 2 g calcium carbonate/d. The primary study endpoint was genome-wide gene expression in biopsy specimens of the rectosigmoid colonic mucosa. Serum and urinary calcium concentrations were also measured.

RESULTS: Changes in urinary calcium accurately reflected calcium consumption. The WD induced modest upregulation of genes involved in inflammatory pathways, including interferon signaling, and calcium supplementation reversed these toward baseline. In contrast, supplementation of the WD with 1,25(OH)2D3 induced striking upregulation of genes involved in inflammation, immune response, extracellular matrix, and cell adhesion. Calcium supplementation largely abrogated these changes.

CONCLUSIONS: Supplementing 1,25(OH)2D3 to a WD markedly upregulated genes in immune response and inflammation pathways, which were largely reversed by calcium supplementation. This study provides clinical trial evidence of global gene expression changes occurring in the human colorectum in response to calcium and 1,25(OH)2D3 intervention. One action of 1,25(OH)2D3 is to upregulate adaptive immunity. Calcium appears to modulate this effect, pointing to its biological interaction in the mucosa. This trial was registered at clinicaltrials.gov as NCT00298545 Trial protocol is available at http://clinicalstudies.rucares.org (protocol numbers PHO475 and PHO554).

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