The Role of Legumes in Weight Management, Insulin Resistance and Colon Cancer Prevention

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ABSTRACT: Penn State University and the National Cancer Institute are currently conducting the Legume Inflammation Feeding Study (LIFE), a randomized, crossover design, controlled feeding study. The purpose of this study is to evaluate the effects of a low-glycemic, legume-enriched high fermentable fiber diet on measures of inflammation and insulin resistance. Both inflammation and insulin resistance have been associated with colon cancer. Study participants may choose to partake in an optional weight-loss phase which will evaluate the effects of the dry bean diet on weight loss and associated hormonal changes. This paper will focus on the preliminary results of the optional weight loss phase and discuss the relationship of weight loss with insulin resistance and colon cancer. Volunteers for this study are men between ages 35-75 who are classified as either insulin resistant or non-insulin resistant. During the first two phases of the study, participants spend four consecutive weeks eating the control diet and four weeks on the legume test diet, in random order. In the optional phase, participants are given limited guidance for eliminating calories. They are asked to eat all the bean dishes, but they may limit or cut out any of the remaining foods. Preliminary results indicate that subjects had an average 8.9 pound weight loss in four weeks.

Introduction

The most recent 1999-2000 National Health and Nutrition Examination Survey (NHANES) reported that approximately 64% of American adults are considered overweight, or have a Body Mass Index (BMI) ≥ 25 (Seagle et al, 2001). Of these, about 1/3 of these adults are considered obese (BMI >30) (Seagle et al, 2001). Significant evidence shows that obesity (especially in the abdominal region) is a major risk factor for insulin resistance. This, in turn, is a major risk factor for non-insulin dependent diabetes mellitus (NIDDM) (NIH Pub. 06-04893, 2006). Several cohort studies have shown that there is a positive association with NIDDM and colon cancer (Giovanucci et al, 2007). Finally, colon cancer is currently one of the top 5 leading causes of cancer deaths in the United States (Giovanucci et al, 2007).

This cascade of events emphasizes the fact that obesity is a multi-faceted health disorder. As research progresses it is clear that the state of one's health is dependent on multiple factors. The complex web of optimal health, disease prevention and the origin of disease further complicate the treatment process. The treatment itself can be considered multi-faceted and perhaps should be viewed as a scale of treatment rather than a pinpoint trial.

It is in this light that the current study examines weight loss. As weight decreases perhaps the dangerous cascade of health events can be halted and perhaps, even reversed.

As seen in the Diabetes Prevention Program (DPP), lifestyle changes, including weight loss, reduced the risk of developing type 2 diabetes among overweight people by 58 percent. Many who had insulin resistance were also able to reverse this condition (NIH Pub.06-4893, 2006).

However, effectively losing weight remains the major obstacle. In this study a diet rich in legumes is being evaluated for its ability to aid in weight loss. Plasma serum and fecal samples will be evaluated to determine any impact from the resulting weight loss on other factors, such as inflammation, that may influence carcinogenesis in the colon. As such, the main hypothesis of the Legume Inflammation Feeding Study (LIFE) is that a high legume, low glycemic diet will help to lessen the inflammation caused by obesity and insulin resistance which may contribute to the formation of adenomas in the colon, the precursors to colon cancer.

There are three phases to this study. The first two phases include eating from two diets. One diet is based on the average American diet which includes foods that are low in fiber and have a high glycemic index. The test diet is a low glycemic, legume enriched high fermentable fiber diet (fig. 1). Each menu on the test diet includes approximately 1 ½ cups of beans per day. Dry beans included in this study are red kidney, black, navy and pinto beans. The third phase is an optional weight loss phase in which the volunteers continue eating the legume diet.

Fig.1

Example Menus

	Low GI	**High GI**
Breakfast	**Omelet**	**Waffles & syrup**
	Oat bran bread	**Turkey sausage**
	Peanut butter	**Cranberry juice**
Lunch	**Black bean soup**	**Ham sandwich**
	Grapes	**Canned peaches**
	2% Milk	**1% Milk**
	Vanilla pudding	
Dinner	**Pork stir fry**	**Pork stir fry**
	Brown rice	**White rice**
	Three bean salad	**Bread/margarine**
Snack	**Apple**	**Jelly beans**

Hartman, TJ, Personal communication.

Methods

The study has been conducted in accordance with the Institutional Review Board at the Pennsylvania State University. All participants were informed of their rights and written consent was obtained prior to controlled feeding. Males between ages 35-75 years old with a Body Mass

Index (BMI) 25.0-34.9 kg/m^2 were recruited from a local outpatient gastroenterology facility. All subjects had a colonoscopy within two years prior to study participation. All participants were assigned to one of four groups based on colonoscopy results (+/- adenomatous polyps) and if they were insulin resistant or non-insulin resistant. For the purpose of this paper, subjects who participated in the weight loss phase were categorized as either insulin resistant (IR) or non-insulin resistant (NoIR). A subject was classified as insulin resistant if he had a value ≥2.61 as determined by the Homeostasis Assessment Model (HOMA-IR) [*fasting serum insulin x fasting glucose/ 2.25*] (Monzillo et al, 2003).

Potential subjects were excluded if they had any of the following: cancer, heart disease, kidney disease, diabetes or other serious medical condition, surgical resection of adenomas, bowel resection, polyposis syndrome, inflammatory bowel disease, regularly smoked in year prior to study, any condition that would substantially limit compliance with the dietary protocol, taking any medication that affects inflammation markers, insulin, glucose or lipids.

After acceptance into the study, participants were randomized into the controlled feeding portion of the research. Participants were provided all foods and caloric beverages in amounts determined by individual caloric needs. For the first two phases, caloric intake is adjusted for each participant to maintain weight. All foods and beverages were prepared at the General Clinical Research Center, Penn State University.

Both diets were isocaloric with similar macronutrient profiles (fig.2). For DP1 and DP2, participants were given menu checklists to ensure receipt of foods and asked to consume all foods received and return all food containers with any uneaten foods or beverages (to measure compliance).

Figure 2.

Nutrient profiles averaged over one week

Nutrient	Low-GI Diet	High-GI Diet
Glycemic Index	**37**	**69**
Glycemic Load	**80**	**138**
Total Fat (% kcal)	**35**	**34**
SFA (% kcal)	**12**	**11**
Protein (% kcal)	**19**	**18**
Carbohydrate (% kcal)	**48**	**49**
Fiber (g)	**39**	**17**
Cholesterol (mg)	**142 mg**	**180 mg**

Hartman, TJ, Personal communication

In the optional weight-loss phase, participants were instructed to eat only until satisfied, starting with the bean dish first. Afterwards, they could reduce or eliminate any of the remaining foods and beverages. Weight was measured and logged daily. Participants were also asked throughout the study to fill out daily monitoring forms indicating any alcohol or extra non-study foods consumed and any study foods not consumed. GCRC staff also monitored returned food containers. Participants were asked not to alter physical activity levels for the duration of their time in the study.

Blood samples were collected before, during (mid-point), and after each diet phase and will be analyzed when all samples have been collected. Plasma serum will be analyzed for cholecystokinin (CCK), leptin, ghrelin, insulin, glucose, C- reactive proteins, C-peptides, cytokines and lipids.

Results

At the time of project submission, 59 of the participants completed both required phases of the study (n=69). Of these, 38 completed the optional weight loss portion (DP3). Six participants were still in progress. Three men were dropped from the study for reasons of gastrointestinal upset and/or time constraints. One man dropped out before beginning DP1. Overall, across both the IR and NoIR groups, participants lost an average of 8.5 pounds (+/- 5.8) over the four week weight loss period.

The IR group (12 of 14) had 86% of participants lost greater than or equal to 5 pounds. Values less than 5 lbs were considered a zero-weight loss as the human body can fluctuate +/- 5 lbs in a single day. There was an average weight loss of 10.4 lbs (+/- 7.11). In the NoIR group (16 of 24) 67% of the participants lost ≥ 5 lbs. The No-IR group had an average weight loss of 7.4 lbs (+/- 4.70).

Discussion

Our results suggest that consumption of a high legume, high fiber, low glycemic index diet was able to facilitate weight loss in a group of older men. For 38 subjects who completed the four-week weight loss diet period, weight loss was 8.5 (+/- 5.8) pounds on average. Moreover, 28 of the 38 participants who completed this diet period lost five pounds or more.

The greater weight loss among the IR group could possibly be due to the higher baseline BMI (30.79 +/- 3.29) and waist circumference(103.10 cm +/- 7.72) compared to the No-IR group: BMI 26.84 +/- 2.92 and waist circumference 93.52 cm +/- 8.64 (Zhang et al, 2007). Motivation due to increased health risks may have motivated some individuals to be more conscientious of types and amounts of food.

Overall, other factors that may have attributed to the weight loss of both groups could be CCK levels, trypsin and amylase inhibitors and the high fiber/ low glycemic nature of the legume diet (Rizkalla et al, 2002).

Cholecystokinin (CCK) is released from the pancreas in response to the presence of protein and lipids within the small intestine. This gut peptide is associated with meal reduction and cessation (Woods et al, 2000). Dry beans contain minor trypsin-inhibitor (TI) activity (Champ, 2002). Although this activity is reduced when the beans are cooked and rinsed, enough is still present to extend CCK secretion (Bourdan et al, 2002). This can result in a greater feeling of satiety for a longer period of time (Burton-Freeman et al, 2002)).

Trypsin is a digestive enzyme secreted by the pancreas that normally breaks down proteins. The presence of TI may possibly reduce absorption of nutrients by inhibiting the cleaving of amino acids in proteins. Another enzyme possibly affected by legumes is amylase. High amounts of amylase inhibitors are present in red kidney beans. Amylase inhibitors are sold commercially as “starch blockers” although these preparations have not been shown to be affective in clinical trials (Champ, 2002).

The low glycemic, high fiber legume diet may be acting upon several other digestive mechanisms to control weight. First, adiponectin, an adipose-secreted cytokine, improves insulin sensitivity. Low plasma levels are present in individuals with type 2 diabetes. In a study by Qi et al (2005), high GI/load is associated with a decrease in plasma adiponectin. An increased consumption of cereal fiber, such as in the legume diet, plus magnesium supplements were associated with increased levels of adiponectin and the corresponding increased insulin sensitivity could result in better disposal of plasma glucose. Therefore more glucose is immediately broken down as energy rather than deposited in adipose tissue. This study could also boost the argument for the use of a low-glycemic diet in weight loss.

Further, fiber can affect how much food an individual consumes in a variety of ways. Foods with a low glycemic index are high in fiber which may aid in decreased postprandial plasma glucose and insulin (Behall et al, 2006; Potter et al, 1981). This results in a more gradual release of energy and prolonged satiety (duration of time between meals) (Burton-Freeman, 2000; Rizkalla et al, 2002). Higher fiber concentrations can also slow gastric emptying so that satiety hormones remain elevated for longer periods (Burton-Freeman, 2000). High fiber, low glycemic foods also prolong chewing time (Burton-Freeman, 2000) giving the feeling that more food has been consumed.

Much is still unknown of the mechanisms for weight loss when including legumes or other high fiber foods in the diet. For example, Rizkalla et al. (2002) conclude that the use of a low glycemic diet may result in favorable weight loss in the abdominal region. Also, Higgins et al, (2004) suggests that diets high in resistant starch, such as that found in legumes, can promote lipid oxidation. Further examination is required for both of these hypotheses to be fully explained

Since this study’s main purpose is to monitor markers of inflammation within the blood and colon, and not to study how weight-loss is aided by the legume biochemistry, further study needs to focus on the latter. However, there is still room for legume research in the realm of cancer studies. One such aspect may be the relationship of legumes and trypsin activity with carcinogenesis in the colon.

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