An investigation into pulse fibre fermentation and nitrogen excretion in patients with chronic renal failure

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SPG Contributions	Project Status	Duration/Timeline of Project (Year to Year)	Total Project Cost
$171,040.00	Completed	May 2009 – April 2012	$171,040.00

Project Description

Chronic kidney disease (CKD; known as chronic renal failure in Canada) is a costly co-morbidity of diabetes and hypertension. More than eight million people in the U.S. have CKD. CKD can progress to end-stage renal failure where the only treatment options are dialysis and transplant. Health costs for these treatments in the USA were $22.8 billion in 2001.

With the progression of CKD comes uremic syndrome where patients have high levels of blood urea (and other waste products from protein metabolism) due to the inability of the kidneys to excrete these waste products. While the current nutrition therapy for CKD focuses on low to moderate protein intake, high fiber intake, restricted sodium and phosphorous intake and high calcium intake, there are limited guidelines on how to achieve this diet. Poor patient compliance and malnutrition is seen in many individuals. The restriction on phosphorous intakes means many good sources of dietary fibre such as pulses, bran cereals, and whole grains, as well as many fruits and vegetables may be excluded from a CKD diet due to potassium restriction.

The researchers hypothesized that the lack of dietary fibre in the renal diet leads to constipation and contributes to uremic syndrome. The lack of dietary fibre leads to a decrease in fermentable carbohydrate reaching the colon, a reduced proliferation of bacteria, and thus a reduced requirement for nitrogen. Subsequently there is reduced movement of urea from the blood to the colon, as urea is the main substrate for bacterial protein synthesis in the colon. Previous research had shown that fermentable fibre supplementation functions to decrease blood urea nitrogen and increase fecal nitrogen in patients with CKD.

Pulse fibre fractions, unlike their pulse seed sources, are low in phosphorous and may be appropriate for those on a renal diet. This clinical trial studied the effect of the pulse fibre fractions on blood urea nitrogen, urinary nitrogen excretion, fecal nitrogen excretion, and fecal microorganisms as well as markers of metabolic stress and inflammation in patients with CKD.

Hypothesis: Dietary supplementation of patients with CKD with a fibre combination including a pulse source will result in significant depression of blood urea levels, shifting nitrogen from urine to fecal excretion and reduce uremic symptoms, improvement in constipation and general quality of life.

Fermentation of pulse fibres may reduce serum markers of inflammation and improve serum antioxidant capacity.

Three clinical studies were conducted to investigate the effects of a mixed fibre source in stage three to five CKD patients:
1. A six-week single-blind cross-over study to determine the effects of adding foods fortified with 23g/d functional fibre versus low fiber foods to diets of patients with CKD. Fifteen adults (9F, 6M; 66±15y) Participants were provided with four servings per day of commercially-available foods (cereal, cookies and snack bars) without added fibre for two weeks, followed by similar foods with 23g per day functional fibre (pea hull, inulin an soluble corn fibre) for four weeks. Pre and post blood samples were tested for blood urea nitrogen, serum creatinine, fasting blood glucose, and lipid profile. Participants also completed validated Quality of Life (QoL) assessment tools and Gastrointestinal Symptom Rating Scale (GSRS) questionnaires to assess physical and mental functioning and GI symptoms, respectively.

2. A single-blind intervention with an escalating fiber regimen. Thirteen participants enrolled in study (7F, 6 M; 65 yrs±12 yrs). Participants in stage three to five of CKD consumed control study foods (muffins) with no fiber supplement (sucrose as control supplement) for a two week control period, followed by a four week period of consuming muffins fortified with pea hull fiber and control supplement (sucrose) followed by six weeks of higher fibre treatment (10 g pea hull + 15 g inulin). Three blood samples were collected in the control period, two blood samples were collected in the pea hull fibre period (four week) and three blood samples were collected in the six week higher fibre period. QoL questionnaire, food records, bowel movement frequency questionnaire, and anthropometric measurements were completed during the study.

3. This 45 day study was designed to determine whether pea hull fiber, in addition to a high protein diet, could redirect nitrogen to the feces. Healthy adult males (>18 yr) who typically consume a high protein/low fibre diet were recruited for this study. The 15-day control period entailed a high protein/low fibre diet, followed by 15 day diet of high protein/high fibre (20g/d), and followed by a final 15 day period of high protein food without fibre supplementation. All food was supplied to participants during the study. Participants collected all stools and urine during the last three days of each 15 day study period for laboratory analysis to determine changes in fecal and urinary nitrogen output.

Outcome

Study No.1: Six week single-blind crossover study: consumption of pea hull fiber fortified foods resulted in: 1) Decreased blood urine nitrogen (BUN) levels by 9.8% and serum creatinine by 7.6%
2) No changes in body weight, fasting blood glucose or lipid profile
3) Daily bowel movement frequency increased
4) Increased fibre intake (mean intake increased from 11.8 to 22.4 g/d) with no change in protein or energy intake in CKD individual
5) Increased physical health composite score
6) Consuming foods with added fibrE had:
i) No significant effect on microbial diversity, structure of the microbiota or numbers of lactic acid bacteria or bifidobacteria
ii) Did cause changes in proportion of individuals containing specific operational taxonomical units within the microbiota

Study No.2: A single-blind intervention with an increasing fibre regimen
1) Bowel movement frequency significantly improved on both the low fibre (10g/d pea hull fiber) diet and high fibre diet (10 d pea hull fibre + 15.0 g/d inulin) compared to the no fibre diet
2) No significant difference between periods for blood urea nitrogen, ammonia, cystatin C, creatinine, CRP, and eGFR
3) Mean total plasma p-cresol between control and post interventions was -37%.
4) No significant changes noted in overall quality of life

Study No.3: Effect of pulse fibre on the redirection of nitrogen from urine to feces
1) Median change in total urinary nitrogen content or total fecal nitrogen content was not significantly different between the 3 intervention periods (high protein diets with a) low fibre b) high fibre c) low fibre, each for 15 days.
2) No significant differences noted for content of short chain fatty acids (SCFA) between the WKUHH interventions but a larger sample population is needed
i) Results suggest an increase in SCFA with added fiber. (Total SCFA increased 10.0 mg/d feces in low fibre intervention to 12.1 mg/g of feces during pea hull intervention.
3) Microbiota Analysis
i) High protein diet negatively impacted Bifidobacteria with potential improvement with pea hull fibre
ii) DNA amplification, quantification and sequencing showed individualized microbiota diversity with no clear pattern of change noticeable during the different interventions
iii) Further data analysis using Heat Maps and UniFrac statistical tools comparing the diversity and similarities of specific OTU (operational taxonomic units-a microbial diversity unit) found in the gut microbial community. Results suggested that pea fibre may enhance some
bacterial species including butyrate-producing bacteria.

Pea hull fibre supplementation of the diets of CKD patients resulted in significant improvements in bowel function with no adverse gastrointestinal symptoms.

Findings suggest that foods with added pea hull fiber may have positive impacts on specific components of quality of life and clinical markers of kidney function in CKD patients.

Findings suggest high protein diet is detrimental to bifidiobacteria and pea hull fiber may exhibit a slight protective effect. Pea hull may enhance a number of bacterial species including butyrate-producing bacteria.

However, results suggest pea hull is not effective in rerouting nitrogen from urinary to fecal excretion, most likely due to its limited fermentation.

Opportunities for new uses of pea products (pea hulls) for niche health markets.

Research Objective

OBJECTIVE 1
To determine the effectiveness of various pulse fibre sources, the dose response of the most effective pulse fibre, and the the long term effectiveness of a single pulse fibre, or combination on uremia, kidney infection and nutritional status.