Title: Protein Intake in Potentially Insulin Resistant Adults: Impact on Glycemic and Lipoprotein Profiles **- NPB #01-075**

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I. Abstract:

Adults who are insulin resistant may improve their blood sugar control without elevating blood lipids if they consume a high protein diet, such as lean pork. To address this hypothesis, we examined cross-sectional data from the Third National Health and Nutrition Examination Survey (1988-1994). A total of 13,794 adults met at least one of the following criteria that places them at increased risk for insulin resistance: overweight (BMI ≥ 27); abdominal obesity (waist circumference >97 cm for women or 102 cm for men); family history of type 2 diabetes; elevated fasting blood sugar (>110 mg/dL); or moderately elevated serum triglyceride (150-499 mg/dL). Subjects were divided into quartiles of total and animal protein intake. Differences in blood sugar and lipid concentrations by protein quartiles were analyzed using SUDAAN after adjusting for sex, age, BMI, waist circumference, fat, carbohydrate, and alcohol intake, physical activity, and number of risk factors. Adults who ate the most total and animal protein intake had the lowest serum total and high density lipoprotein (HDL) cholesterol. Adults who were in the second lowest quartiles of total and animal protein intake had the lowest insulin concentrations ($P < 0.05$). Serum low density lipoprotein (LDL) cholesterol, triglycerides, glucose, and glycated hemoglobin were not significantly related to protein intake after adjusting for the confounding variables. Therefore, total and animal protein intakes were not consistently associated with blood sugar control or indicators of cardiovascular risk.

II. Introduction:

Dietary patterns of individuals are influenced by various factors, such as cultural and ethnic background and religious and philosophical beliefs. Recently Jensen et al. (2000) determined that consumer selection of meat products is influenced by knowledge and attitudes about diet and meat products. According to information provided by the National Pork Producers Council, pork sales depend on consumers' perceptions of the value of pork in a healthy diet.

Studies show that diets high in saturated fats and simple sugars promote increased insulin resistance, but the effect of protein on insulin resistance is not well-studied. Low calorie diets and weight loss are associated with reduced insulin resistance. In recent years, dietary guidance for weight loss focused on encouraging adults to lower their fat intake, however too much emphasis on increasing carbohydrate intake may worsen blood sugar control in adults who are insulin sensitive. The consumption of very lean meats as part of low fat diets has resulted in reduced blood lipid concentrations. Therefore, diets that are lower in fat and carbohydrate but higher in protein may promote weight loss with better blood sugar control. Demand for lean pork products should increase if it can be demonstrated that a high protein diet is associated with better blood sugar or lipid concentrations.

III. Objectives:

To examine the relations between protein intake and blood lipid and blood sugar profiles in adults in the Third National Health and Nutrition Examination Survey (1988-1994) who are potentially insulin resistant. Following questions were identified:

1. What is the relation between protein intake and blood sugar profiles (fasting and postprandial glucose and insulin, C-peptide and hemoglobin A1c) in potentially insulin resistant adults?
2. What is the relation between protein intake and blood lipid profiles (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) in potentially insulin resistant adults?

IV. Procedures:

The study used a correlational design. First subjects who met at least one of the identified criteria of high risk for insulin resistance were selected from the Third National Health and Nutrition Examination Survey (1988-1994) data set, which includes a nationally representative sample of the U.S. civilian noninstitutionalized population, based on a complex, stratified, multistage probability cluster sampling design with oversampling of blacks and Mexican-Americans.

Second, the protein intake for the potentially insulin resistant adults was estimated by 24 hour dietary recall. Subjects were divided into quartiles using two classification methods: grams of total and animal protein from a 24 hour recall. (See Table 1)

Third, blood sugar profiles were determined by fasting and postprandial blood glucose and insulin concentrations, and C-peptide concentrations. Hemoglobin A1c, an estimate of blood glucose levels over the past 2-3 months, was also assessed. Blood lipid profiles were determined by concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides in the blood.

Fourth, the association between blood sugar and blood lipid profiles and age, BMI, waist circumference, number of risk factors, and macronutrient intake were determined using Pearson correlation coefficients.

Finally, the blood sugar and blood lipid profiles were compared among adults by quartile of total and animal protein intake. Differences in blood sugar and blood lipid profiles among quartiles of protein intake were determined by analysis of covariance to adjust for potential confounding variables: age, sex, BMI, waist circumference, lifestyle factors (physical activity and alcohol consumption), dietary intake (fat and carbohydrate), and number of risk factors. The data was weighted to account for the complex research design, correct for differential selection probabilities and adjust for non-response by using sample weights, provided by the National Center for Health Statistics. We used SUDAAN (Research Triangle Institute, 2000) software for variance and quartile estimation. P values of <0.05 indicated statistical significance.

V. Results:

After excluding adults who had been diagnosed with diabetes, reported taking insulin or oral hypoglycemic agents, or had very high triglyceride concentrations, 13,794 adults had at least one risk factor for insulin resistance. The average number of risk factors per participant was 1.7. The average age of subjects was 43 years. The average BMI and waist circumference of subjects were 26 kg/m^2 and 90 cm respectively.

Average total protein intake in this sample was 79.4±44.7 gm/day. The average intake of subjects was composed of: 35.5% of total kcal from fat, 14.9% protein (10.1% from animal protein), and 49.7% carbohydrate.

A high BMI was the most common risk factor (71%) for both men and women. Family history was the second most common risk factor for women (38%), whereas elevated serum triglycerides was the second risk factor for men (35%). About half the adults exhibited only one risk factor and about 40% exhibited two risk factors.

In terms of the National Cholesterol Education Program (2001) and American Diabetes Association (1998) criteria, the average total cholesterol and LDL cholesterol were borderline high and near optimal/above optimal respectively. Average HDL cholesterol, triglycerides, and glucose values were within the normal range. Average values were similar for both genders.

Age, BMI, waist circumference, and number of risk factors were significantly correlated with all blood lipid and blood sugar profiles. Macronutrient intakes were significantly but weakly correlated with lipid and blood sugar laboratory values. Total protein intake was negatively correlated with total cholesterol (r= -.05), HDL cholesterol (r= -.09), and glycated hemoglobin (r= -.02). Animal protein intake was negatively correlated with total cholesterol (r= -.03) and HDL cholesterol (r= -.07).

After adjusting for the confounding variables, total cholesterol and HDL cholesterol were significantly higher in the lowest protein quartile compared to the highest protein quartile. However, serum insulin was lowest in the second quartile of both total and animal protein, and serum C-peptide was lower in the second and highest quartiles of total protein (See Table 2 & 3). LDL cholesterol, triglycerides, serum and plasma glucose, and glycated hemoglobin were not significantly different by quartile of protein intake.

The study did not demonstrate a consistent relation between total and animal protein intakes and blood sugar control or blood lipid concentrations. Serum insulin, an indication of insulin resistance, was lowest in adults who were in the second quartile (25^{th} to 50^{th} percentile) of protein intake. However, other indicators of blood sugar control did not differ by quartiles of protein intake. Lower protein intakes were associated with slightly higher total cholesterol concentrations (indicating increased cardiovascular risk) but also slightly higher HDL cholesterol concentrations (indicating decreased cardiovascular risk). Future studies that provide an increased protein intake in controlled clinical trials with insulin resistant adults are needed to determine the effect of protein on blood sugar control and cardiovascular risk.

Reference List

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National Center for Health Statistics. Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988-1994. Vital Health statistics, series 1, No.32. Hyattsville, MD: Public Health Service, 1994.

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Table 1 Total protein and animal protein intake by quartiles

	<25		25-50		50-75		>75	
Variables	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
Total Protein (gm)	36.0	0.21	60.1	0.13	83.7	0.19	139.1	1.35
Animal Protein (gm)	19.3	0.14	38.0	0.10	57.0	0.18	103.7	1.00

Table 2 Differences in lipid and blood sugar profiles by total protein quartiles[1-2]

	<25		25-50		50-75		75-100		
Variables	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.	P
Total Cholesterol (mg/dL)	204.8[a]	1.12	201.0[b]	0.87	201.7[ab]	1.18	197.2[c]	1.03	<0.007
LDL Cholesterol (mg/dL)	126.6	1.01	123.0	1.00	124.7	1.08	122.1	0.80	<0.33
HDL Cholesterol (mg/dL)	52.3[a]	0.45	52.7[a]	0.41	50.9[b]	0.42	48.8[c]	0.32	<0.05
Triglycerides (mg/dL)	129.7	2.42	127.4	2.49	130.9	2.01	132.0	2.33	<0.22
Serum Glucose (mg/dL)	92.4	0.39	92.4	0.39	92.2	0.41	92.4	0.47	<0.95
Plasma Glucose (mg/dL)	94.7	0.41	94.4	0.29	94.2	0.41	94.6	0.38	<0.57
Serum Insulin (uU/mL)	10.3[a]	0.30	9.6[b]	0.19	10.0[a]	0.25	10.2[a]	0.25	<0.01
Serum C-peptide (pmol/mL)	0.70[a]	0.01	0.65[b]	0.01	0.67[a]	0.01	0.66[b]	0.01	<0.004
Glycated Hemoglobin (%)	5.23	0.02	5.23	0.02	5.22	0.01	5.20	0.02	<0.86

[1]Means in a row with different superscripts are significantly different (p<.05)
[2]Model includes following covariates: age, sex, BMI, waist circumference, lifestyle factors (physical activity and alcohol consumption), dietary intake (fat and carbohydrate), and number of risk factors

Table 3 Differences in lipid and blood sugar profiles by animal protein quartiles[1-2]

Variables	<25 Mean	<25 S.E.	25-50 Mean	25-50 S.E.	50-75 Mean	50-75 S.E.	75-100 Mean	75-100 S.E.	P
Total Cholesterol (mg/dL)	202.9[a]	1.13	201.3[a]	0.92	202.7[a]	1.18	197.5[b]	1.03	<0.002
LDL Cholesterol (mg/dL)	124.8	0.99	123.7	0.97	125.2	1.16	122.4	0.79	<0.20
HDL Cholesterol (mg/dL)	52.0[a]	0.42	52.0[a]	0.50	51.6[a]	0.44	48.9[b]	0.33	<0.03
Triglycerides (mg/dL)	131.2	2.50	127.8	2.42	129.8	2.12	131.4	2.20	<0.50
Serum Glucose (mg/dL)	92.5	0.34	92.2	0.43	92.2	0.42	92.4	0.45	<0.62
Plasma Glucose (mg/dL)	94.5	0.40	94.5	0.30	94.3	0.40	94.6	0.37	<0.50
Serum Insulin (uU/mL)	10.1[a]	0.27	9.4[b]	0.20	10.2[a]	0.24	10.4[a]	0.23	<0.008
Serum C-peptide (pmol/mL)	0.68	0.01	0.66	0.01	0.67	0.01	0.67	0.01	<0.71
Glycated Hemoglobin (%)	5.23	0.02	5.23	0.02	5.22	0.01	5.20	0.02	<0.22

[1]Means in a row with different superscripts are significantly different (p<.05)
[2]Model includes following covariates: age, sex, BMI, waist circumference, lifestyle factors (physical activity and alcohol consumption), dietary intake (fat and carbohydrate), and number of risk factors