PART XXXI

HYPERTENSION–PHYSIOLOGY 843

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PART XXXII

CARDIOVASCULAR 875

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DIET AND BLOOD GLUCOSE: EFFECTS ON RENAL RESPONSE TO ACUTE DIETARY PROTEIN CHALLENGE IN DIABETICS WITH ELEVATED GLOMERULAR FILTRATION RATE

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Summary

The glomerular filtration rate (GFR) response to a meat meal containing 70–100g of protein was measured in five insulin dependent diabetic patients with persistently elevated GFR. Studies were performed after a period on a low protein diet and one of an ad libitum diet. On normal protein intake tests were performed twice during euglycaemia and hyperglycaemia. Nine non-diabetic control subjects were studied on an ad libitum diet.

Basal GFR was significantly reduced in all insulin dependent diabetic patients after a period of a low protein diet (mean ±SD 151±13 to 136±17ml/min/1.73m^2; $p<0.02$). Mean GFR rose significantly after the meat meal in controls (107±11 to 120±12ml/min/1.73m^2; $p<0.01$). Insulin dependent diabetic patients showed an abnormal pattern of response to acute protein challenge during hyperglycaemia (basal GFR (mean ±SD) 152±12 to test GFR 156±16ml/min/1.73m^2) two subjects showing a rise, two a fall and one no change. Euglycaemia tended to normalize the response (151±13 to 161±18ml/min/1.73m^2) which showed a rise in four out of five patients.

After a period of low protein diet, all five subjects showed an increase in GFR after the meal (mean 136±17 to 149±15ml/min/1.73m^2; $p<0.02$).

Ambient plasma glucose concentration has an important modulating effect on the renal response to dietary protein challenge in insulin dependent diabetic patients with elevated GFR. Previous diet affects basal GFR and has a further effect on the response to a meat meal.

Introduction

Up to 30 per cent of insulin dependent diabetic patients have an elevated glomerular filtration rate [1], and this is thought to be a potentially deleterious situation [2]. Dietary modification with reduction of protein intake can affect GFR in normal subjects [3], and has been reported to slow the rate of progression of established renal failure [4]. Conversely, protein loading acutely

increases GFR in normal subjects [5]. The role of dietary protein as a modulator of GFR in diabetes, and its inter-relationships with plasma glucose are as yet unexplained.

Subjects and methods

Five male insulin dependent diabetic patients aged between 23–39 years were selected on the basis of previously demonstrated elevation of GFR (normal range in our laboratory 84–135ml/min/173m^2) measured as ^{51}Cr EDTA clearance [6]. Nine non-diabetic control subjects matched for age and sex served as control. Diabetic patients were admitted the night before the study and an intravenous infusion of insulin started to maintain plasma glucose between 3.5 and 6mmol/L. This was continued throughout the study. During hyperglycaemia experiments a graded infusion of dextrose 50g/dl was superimposed to raise plasma glucose by approximately 7mmol/L. Studies were performed under water diuresis with constant infusion of inulin and PAH. Four 15 minute periods were used for measurements of basal PAH and inulin clearance. Thirty minutes was taken to eat the protein meal (70–100g) given as grilled steak, followed by nine 20 minute periods afterwards. The mean of the clearance periods over a full hour were used for calculation. Diabetic patients performed the euglycaemic study after both normal diet and three weeks of low protein diet (approx 40g/day). During this period, the diet was supervised by a nutritionist and plasma and urine samples were taken for estimation of urea and creatinine excretion.

Compliance with the low protein diet was good, as assessed by diet history and plasma and urinary urea and creatinine. Details are given in Table I.

TABLE I. Total daily protein intake, plasma and urine urea and creatinine in five insulin dependent diabetic patients with glomerular hyperfiltration

	Normal protein diet	Low protein diet
Total daily protein (g/day)	98.1±17	44.6±7**
Plasma urea (mmol/L)	4.7±0.2	3.2±0.7*
Urea excretion (mmol/24h)	480±129	221±76*
Plasma creatinine (μmol/L)	79±9	78±8
Creatinine excretion (mmol/24h)	13.6±5	11.9±6

Data are given as mean ±SD
** = $p<0.02$
* = $p<0.05$

Results

In the insulin dependent diabetic patients, GFR fell from 151±13 to 136±17ml/min/1.73m^2 ($p<0.02$) after three weeks of low protein diet.

After an acute protein challenge, GFR in controls arose from 107±11 to 120±12ml/min/1.73m^2 ($p<0.01$). During normal diet, GFR in diabetic patients in hyperglycaemia showed a mixed response rising in two and showing a fall or no change in three (mean ±SD 152±12 vs 156±16ml/min/1.73m^2 ns). During euglycaemia, the response was more normal rising in four and falling in just one (mean ±SD 151±13 vs 161±18ml/min/1.73m^2). After two weeks of low protein diet, however, the response was completely normalized, rising in all diabetics (136±17 vs 149±15ml/min/1.73m^2; $p<0.02$) the GFR increment was similar to that of the control subjects (15±6 vs 11±5ml/min/1.73m^2; Figure 1).

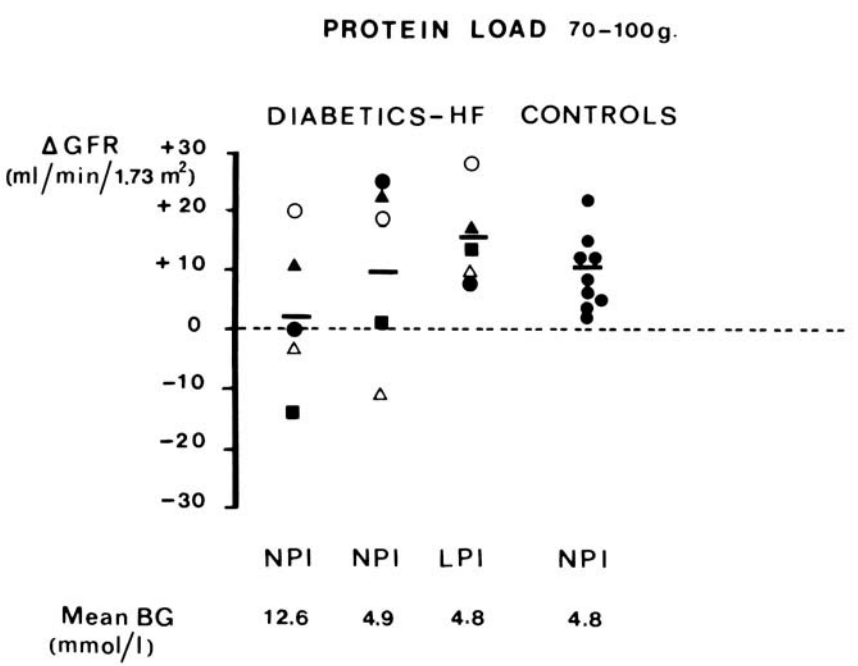

Figure 1. Changes in GFR in five insulin dependent diabetic patients with glomerular hyperfiltration (Diabetics - HF) and nine normal controls in response to a protein load. The protein intake in the weeks preceding the test are indicated NPI = normal protein intake and LPI = low protein intake. Blood glucose values represent the mean blood glucose during the test

Discussion

Ambient glycaemia and dietary proteins both seem to modulate GFR in hyperfiltering diabetic patients.

Our data show that basal GFR is strongly influenced by low protein intake, whereas short-term, overnight normoglycaemia has only a minimal effect on it. The response to a protein challenge is greatly disturbed during hyperglycaemia and euglycaemia tends to normalize it. Moreover a period of low protein diet contributes to total normalization of the pattern of the glomerular response to an acute protein challenge.

Dietary factors may be important co-modulators of glomerular function with glycaemic control, and modification of these may have important ramifications in the prevention of diabetic renal disease.

References

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