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THE EFFECT OF DIETARY PROTEIN QUALITY IN EXPERIMENTAL RENAL DISEASE

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Summary

The quantity of dietary protein has an important influence upon the course of renal disease, and this study compares the effects of a vegetable protein (soya) and an animal protein (casein) upon experimental renal disease in rats. Those animals fed soya demonstrated improved survival, less proteinuria, less renal hypertrophy and less histological glomerular damage compared to animals fed casein. We conclude that the type, as well as the quantity, of dietary protein can influence the progression of renal disease.

Introduction

Renal function in a number of renal diseases will decline at a predictable rate, and the ultimate outcome is usually renal scarring and glomerulosclerosis. A reduction in the quantity of dietary protein has been shown to modify the decline in renal function in some renal diseases and a reduction in 'glomerular hyperfiltration' may be the mechanism responsible [1,2]. High levels of dietary protein intake will increase renal blood flow and elevate the glomerular filtration rate, and this alteration in renal haemodynamics appears to be deleterious to the glomerulus when renal mass is reduced. In addition to the quantity of dietary protein intake influencing the glomerular filtration rate (GFR), the type of protein also appears to be important, as vegetarians have been shown to have lower GFRs than omnivores [3,4]. This study compares the effects of different dietary proteins, i.e. vegetable vs animal (soya and casein), upon the progression of experimentally induced renal disease in the rat.

Methods

Forty-six female Wistar rats weighing 160 to 215g were used in the study.

At the start the animals were bled for estimation of baseline parameters and then maintained on a standard laboratory diet. One week later a right

nephrectomy and partial infarction (approximately 30%) of the left kidney was undertaken as a one stage procedure. The animals were than randomly allocated to receive one of the four experimental diets to commence the following day. At two weekly intervals the animals were placed in metabolic cages for collection of 24 hour urine samples, which were analyzed for urea, creatinine and total protein. Also at these times blood samples were obtained for estimation of serum urea and creatinine. The animals were maintained on the experimental diet for three months after which time they were sacrificed. The remnant kidney was removed, and placed in a prepared container with 10% formalin. The experimental diets, which differed in their protein contents were:-

Diet A (n=11) - 24% casein
Diet B (n=12) - 12% casein
Diet C (n=12) - 24% soya
Diet D (n=11) - 12% soya

The amino acids which differed most widely between the diets at the 24 per cent level are shown in Table I. The sodium, potassium, vitamin and trace element content of the diets were identical and they were isocaloric.

TABLE I. Dietary constituents of 24 per cent soya and 24 per cent casein diets showing the major amino-acid differences (in percentages)

	24% Soya	24% Casein
Arginine	2.43	0.97
Aspartic Acid	2.84	1.43
Proline	1.29	3.07
Glycine	1.10	0.46
Alanine	1.17	0.67
Sodium	0.5	0.5
Potassium	1.1	1.1
Phosphate	0.5	0.5
Energy (kJ/kg)	12	12

Twenty-five grams of dry food was allocated to each animal per day, and mixed into a paste with deionized water. The food remaining each day was weighed, and the quantity of food taken calculated.

If any animal during the study period became unwell, or lost more than 15 per cent body weight in a two day period, the animal was sacrificed and the remnant kidney excised and placed in formalin. Two 4μ paraffin embedded sections of the remnant kidneys were stained with PAS and haematoxylin-eosin, and examined by light microscopy, without knowledge of the animal's group.

All results are shown as mean ± standard error of the mean, and statistical analysis was performed using the analysis of variance.

Results

Survival, weight gain and food consumption (Table II)

The survival of animals ingesting the soya diets was significantly higher than those animals ingesting casein ($p<0.05$). The weight gained by animals in groups A and B (24% casein and 12% casein) was significantly higher than those animals in groups C and D, (24% soya and 12% soya) at the end of the study period ($p<0.001$). The difference was due to the weight gain during the first four weeks of dietary treatment, as during the subsequent eight weeks there was no significant difference in the rate of weight gain between the four groups.

Animals in Group D (12% soya) consumed significantly more food than animals in other groups throughout the study period ($p<0.001$)

TABLE II. Percentage survival, weight gain and food consumption in rats subjected to a reduction in renal mass on differing diets

Group	Percentage survival	Weight gain (g) at 3 months	Food consumption (g/day)
A (n=11)	63.6	28.6±4.7	12.7±0.5
B (n=12)	58.3	19.3±2.3	13.7±1.0
C (n=12)	100.0	8.3±2.9	15.9±0.8
D (n=11)	90.9	11.5±2.8	22.3±0.5

Renal function (Table III)

During the study the quantity of urine passed by animals in group A was signficantly higher than other groups ($p<0.01$). Earlier in the study, animals in group B tended towards a higher urine excretion rate, but at three months there was no difference between groups B, C or D.

The creatinine clearance of groups A and B two weeks after commencing dietary treatment was significantly higher than groups C and D ($p<0.01$);

TABLE III. Renal function, kidney weight and percentage abnormal glomeruli in rats subjected to a reduction in renal mass on differing diets

Group	Urine volume ml/24hrs	Creatinine clearance ml/min/100g body weight	Urea excretion mmol/24hrs 100g body weight	Serum urea mmol/L	Proteinuria mg/24hrs	Remnant kidney g/100g body weight	Percentage abnormal
A	31.1±3.9	0.44±0.03	6.6±0.3	12.8±0.9	98.7±34.0	0.66±0.04	73.4±6.1
B	19.9±2.9	0.39±0.02	2.8±0.3	7.6±0.4	63.8±17.7	0.59±0.04	66.8±4.4
C	21.2±1.7	0.38±0.02	3.5±0.1	7.7±0.2	30.4±5.1	0.46±0.01	44.1±3.9
D	19.7±1.1	0.37±0.02	2.2±0.1	5.2±0.1	35.5±6.7	0.46±0.01	45.7±5.0

however, at the end of the study period there was no significant difference between the groups.

The urea excretion of animals remained stable throughout the study. Those animals on the 24 per cent protein diets having significantly higher values than animals on the 12 per cent protein diets ($p<0.005$), and at each level of protein intake values for animals on the casein diets were higher than animals on the soya diets. This was reflected by values for serum urea, as groups A and D differed significantly from groups B and C ($p<0.005$).

No significant difference was found between the groups for serum albumin, calcium, phosphate or haematocrit after three months.

Proteinuria, kidney weight and histology (Table III)

The amount of protein excreted in the urine per 24 hours remained relatively stable in those animals in groups C and D. The proteinuria of animals in groups A and B was significantly higher than groups C and D after six weeks ($p<0.01$), and the levels continued to rise throughout the study period. The proteinuria of group A was higher than group B.

The weights of the remnant kidneys of animals in groups A and B were significantly higher than those of groups C and D ($p<0.005$). If remnant kidney weight is expressed as a function of body weight, then groups A and B ($y=0.013x-1.55$) form a significantly different population to groups C and D ($y=0.0041x+0.0517$ ($p<0.001$). There was also a significant correlation between remnant kidney weight and proteinuria ($r=0.75$, $p<0.001$).

A wide range in the severity of glomerular lesions was found on light microscopy, ranging from mesangial expansion to total glomerular obliteration. The percentage abnormal glomeruli found in the remnant kidneys of animals in groups A and B was significantly higher than groups C and D ($p<0.005$). All those animals which did not complete the study showed at least 90 per cent abnormal glomeruli.

Discussion

The results of this study show that when soya is given as the dietary protein source to rats subjected to a reduction in renal mass, those animals will demonstrate improved survival, less proteinuria, less renal hypertrophy and less histological glomerular damage when compared to similar animals fed casein. Possible contributing factors to the altered outcome of the groups might include the amino acid composition of the diet. It has been shown that dietary tryptophan supplementation can reduce the proteinuria in a similar model of experimental renal disease [5].

Alternatively, altered renal haemodynamics may be a contributing factor. In the early stages of the study the creatinine clearance values for animals ingesting casein were significantly higher than those animals ingesting soya and it has been shown, in a similar experimental model, that a sustained high glomerular filtration rate and renal blood flow may be deleterious to glomerular function when renal mass is reduced.

Other factors which may be implicated might include hypertension. However in a similar animal model it has been shown that when hypertension is controlled pharmacologically, glomerular lesions and proteinuria continue to develop [6]. Elevated serum phosphate also appears to be detrimental in renal disease [7]. However in this study the phosphate content of the diets was the same, and there was no significant difference in serum phosphate at the end of the study. The mechanisms that are responsible for the differences seen between the dietary groups need further investigation.

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