Effects of Reduced Protein Intake in Rats with Congenital Polycystic Kidney without Renal Failure

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A low-protein diet (LPD) is able to slow the progression of chronic renal failure in polycystic kidney disease (PKD), as well as in other nephropathies [1 - 3]. Recently, a beneficial effect exerted by LPD on cyst development was demonstrated in mice with autosomal dominant PKD [4].

In this study, the effects of a very LPD was studied in the early phase of PKD male rats, without significant reduction of functioning renal mass.

Animals and Methods

Han:SPRD/cy + rats, a strain of Sprague-Dawley rats with autosomal dominant PKD [5, 6], were used. At 3 months of age, 14 rats were selected and randomized in two age-matched groups: Group 1: 7 rats fed a low-sodium, low-protein (3.3 g\%\) diet supplemented with essential amino acids and ketoacids. Group 2: 7 rats fed a low-sodium, normal protein (18 g\%\) diet. Over the 4-month study period, the two groups were not pair-fed. Creatinine clearance, urinary urea and body weight were evaluated monthly.

At 7 months of age the rats were culled through aortic puncture under anesthesia with sodium pentobarbital (5 mg/100 g b.w., i.p.) and the kidneys were removed for histology and morphometric evaluations. The kidneys were bisected in the coronal plane passing through the hilum, to measure longitudinal diameter. The value of glomerular size for every rat represents the mean of 30 measurements of glomerular diameters, at the vascular pole.

For the evaluation of PKD degeneration rate, the following grading scale was used: grade 0: no cysts and no dilated collecting ducts; grade 1: no cysts and some dilated collecting ducts; grade 2: isolated small cysts and dilated collecting ducts; grade 3: large cysts in the whole kidney.

The results were expressed as mean ± SD. Statistical evaluation was performed by Student’s t test for unpaired data. Differences were considered significant when p < 0.05.

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Results

At the end of the study, both in the low-protein and in the normal protein group, 4 out of 7 rats showed large cysts in the whole kidney (grade 3) and the other 3 rats showed isolated small cysts and dilated collecting ducts (grade 2). However, the kidney diameter was smaller in group 1 than in group 2 (19.1 ± 0.8 vs. 21.2 ± 1.7 mm, p < 0.05), as well as the glomerular size (116 ± 4 vs. 127 ± 6 μm, p < 0.01).

Food consumption in group 1 was approximately one-half that in group 2, so that the difference in protein (and energy) intake was very large, as demonstrated by the urinary urea excretion (respectively 43 ± 8 vs. 455 ± 165 mg/24 h, p < 0.001), leading to a lower body weight at the end of the study (301 ± 35 vs. 406 ± 18 g, p < 0.001). As expected, the creatinine clearance in group 1 was lower than in group 2, even when adjusted to body weight (at the end of the study: 3.68 ± 0.70 vs. 4.96 ± 1.02 ml/min/kg b.w., p < 0.05).

Discussion

These data indicate that a very low protein intake did not significantly affect the cyst development grade in the early phase of heterozygous Han:SPRD rats. Actually, the animals on LPD had eaten much less than the rats on normal protein diet; although unwanted, this increased the difference in the effective energy and protein intake between the two groups. It caused remarkable changes in creatinine clearance, glomerular size, and body weight but no beneficial effects on cyst formation (at least with the simple methods used in this study).

In conclusion, a 4-month period of a very low protein intake was not associated with an evident reduction in cyst development grade in rats with congenital PKD model without renal failure. However, we strongly believe that a low-protein intake can be useful in the management of PKD, as well as in other chronic nephropathies, when functioning renal mass is reduced. Indeed, under these circumstances, the LPD can protect the residual renal function through the well-known mechanisms acting at glomerular and tubulo-interstitial levels [7–9].

References


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