Early Tubular Functional Changes in Autosomal Dominant Polycystic Kidney Disease

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Dear Sir,

The loss of renal concentrating ability [1–3] with normal renal function is an early manifestation of the autosomal dominant polycystic kidney disease (ADPKD). In order to estimate whether tubular functional changes are an early event in the course of ADPKD, renal tubular functional tests and sonographic data were compared in 20 ADPKD subjects (1st and 2nd decade of life).

These

subjects were selected by DNA linkage analysis [4–6] and had ultrasonographic studies (3.5-MHz transducers; AUC 940, Ansaldo). Segmental sodium reabsorption was evaluated by the use of free water clearance analysis during maximal diuresis by oral water loads [7]. Serum erythropoietin, urinary enzymes (GGT, NAG) and mic-roalbuminuria were also determined. Ultrasonography showed bilaterally cystic kidneys in all subjects, but 3 (table 1). Serum erythropoietin (GGT

C^3_o =Free water clearance; DSD = distal sodium delivery ($C^3_o + CNa$); FDSR = fractional distal sodium reabsorption ($C^3_o / C^3_o + CNa + \kappa$); N = negative ultrasonography; S = suspected ADPKD according to Sedman et al. [10], as the ultrasonography showed two cortical cysts only in the inferior pole of the left kidney.

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Table II. Hematological, urinary and clinical findings of Bartter-like syndrome in 2 ADPKD subjects

Subject No.	Blood K mEq/l	HC03 mEq/l	PRA ng/ml/h	A ng/dl	Urinary K mEq/24 h	Urinary Na mEq/24 h	BP mm Hg
2.5	31.7	12.1	20.1	46	280	110/80	
3.2	29.8	10.1	26.5	46	400	110/70	

PRA = Plasma renin activity (supine); A = aldosterone.

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and NAG were normal. By contrast, in ADPKD subjects, 2 mean microalbuminuria was significantly higher than in controls (ADPKD = 28.9 ± 22.1 vs. 4.9 ± 3.4 $\mu\text{g}/\text{mg uC}$ in 3 controls; $p < 0.001$). Microalbuminuria values were also high in the 3 cases with negative or suspected sonogra- 4 phic diagnosis of ADPKD (cases 4, 14 and 18 of table 1). Moreover in 30% of the subjects, fractional distal sodium reabsorption was defective (range 0.45–0.78); 2 of these 5 subjects (No. 17 and 18) showed Bartter's like syndrome, as illustrated in table 2. Abnormal tubular functions have previously been observed in ADPKD [1–3], although this finding is in disagreement with renal micropuncture 6 studies revealing normal function of surface proximal and distal tubules in terms of water and solute reabsorption [8].

Also proteinuria has already been reported [9] in 5 of 8 adult ADPKD patients and by Carone [8] who hypothesized a diffusion of interstitial protein across the altered cystic or atrophic tubules. The increased microalbuminuria reported here, with 9 or without ultrasonographic evidence of cysts (table 1) and the defective sodium chloride and potassium trans- 10 port along the distal tubule, indicate possible early renal tubular defects in ADPKD. Such earlier tubular functional changes suggest a variable course of the disease.