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N – ACETYL – β – D – GLUCOSAMINIDASE EXCRETION IN PATIENTS WITH UNILATERAL RENAL AGENESIS OR NEPHRECTOMY IN CHILDHOOD*

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SUMMARY: Tekin N, Kural N, Uslu S. (Department of Pediatrics, Osmangazi University Faculty of Medicine, Eskişehir, Turkey). N-acetyl-β-D-glucosaminidase excretion in patients with unilateral agenesis or nephrectomy in childhood. Turk J Pediatr 1996; 38: 485-490.

Renal functional impairment due to the damaging effect of hyperfiltration of the remnant kidney was evaluated in patients who had been uninephrectomized in childhood or had unilateral agenesis. Sixteen patients (8 male, 8 female) a mean of 7.1 years (1-26 years) postnephrectomy were evaluated. Blood pressure values, clearances of creatinine (Ccr) and phosphorus (Cp), urine osmolality, total protein excretion and NAG (N-acetyl-beta-d-glucosaminidase) excretion were determined. Ccr values were slightly but not significantly lower (90.390 ± 11.223 ml/min) than those of control subjects (110.818 ± 7.755 ml/min). Daily urinary protein excretion adjusted for body surface was significantly higher in the study group ($p < 0.05$). Urinary NAG excretion measured with a spectrophotometric method and described as the Cr ratio was significantly higher in the patients than the control subjects ($p < 0.05$). It was concluded that the damaging effects of hyperperfusion not only involve the glomerulus but also the proximal and distal tubulus. *Key words: nephrectomy, proteinuria, NAG excretion.*

A person can have a solitary kidney congenitally or as a result of nephrectomy for renal disease. On the other hand, some people are renal donors for live transplantation and live with a single kidney for a long time. It has been shown in experimental studies that hyperperfusion of the remnant glomeruli leads eventually to the development of glomerulosclerosis in these patients. Most studies have focused on glomerular functions[1-4]; tubular functions of single-kidney patients have rarely been studied.

In this study, in order to assess the effect of uninephrectomy on both glomerular and tubular functions, we evaluated patients who had been nephrectomized in childhood or had unilateral renal agenesis. Besides clearance tests, the proximal tubulus was also evaluated with N-acetyl-β-D-glucosaminidase (NAG), which is a proteolytic enzyme located in the lysosomal part of the proximal tubulus epithelial cells; raised levels indicate renal tubular damage[5-8].

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Material and Methods

We reviewed the charts of patients who had undergone unilateral nephrectomy during childhood (before 18 years of age) and those with unilateral agenesis. At the time of the study, patients were between two and 31 years of age (median age 15.5 years). The follow-up period with a single kidney was 7.1 years (range 1-26 years). none of the nephrectomized patients had any sign, symptom or laboratory finding of renal functional impairment, hypertension or any systemic disorder causing deterioration in renal function at the time of nephrectomy. Sixteen patients fullfilled those criteria. Fourteen of them were nephrectomized and two had renal agenesis. Table I shows the indications for nephrectomy. At the time of this study, all of the subjects were in good health. Twenty-one control subjects (thirteen female, eight male) with no history of renal disease were also studied. The mean age of the control group was 12.8 years (range 7-18 years).

Table I: Indication for Nephrectomy

No.	Age	Sex	Years post-uninephrectomy	Reasons for nephrectomy
1	10	F	1.5	Left hypoplastic kidney
2	10	M	4	Right hydronephrosis
3	16	M	9	Right xantogranulomatous PN
4	9	M	5	Right kidney aplasia
5	11	M	7	Left xantogranulomatous PN
6	18	F	1	Chronic PN, Right hydronephrosis
7	8	M	8	Left hydronephrosis
8	17	F	7	Chronic PN, right atrophic kidney
9	23	M	12	Left xantogranulomatous PN
10	26	M	8	Chronic PN, right nephrolithiasis
11	2	F	2	Left total multicystic displasia
12	24	F	6	Traumatic hemorrhage
13	20	F	20	Agenesis of the left kidney
14	19	F	1	Multiple nephrolithiasis
15	5	F	5	Agenesis of the left kidney
16	31	M	26	Right hydronephrosis

The subjects greater than 18 years old were considered hypertensive if they had an average systolic blood pressure greater than 140 and/or diastolic greater than 90 mmHg. the prevalence of hypertension in the uninephrectomized group and control group among patients less than 18 years old was compared with the prevalence expected in the general population matched for age and sex.

Laboratory studies: A 24-hour urine sample was collected for the determination of clearances of creatinine and phosphorus (Ccr, P), urine osmolality, total protein

excretion and NAG excretion. Ccr and P were calculated and corrected for body surface area and expressed per 1.73 sqm. Fractional excretion of sodium (FENa), tubular reabsorption of phosphorus (TRP), osmolar clearance and free water clearance were also calculated.

Urinary NAG activity was determined spectrophotometrically[9]. The enzyme activity in each urine sample was expressed as the NAG U/mmol creatinine. Creatinine was measured by the Jaffe reaction[10]. Quantitative urine protein excretion was determined by precipitation with sulfosalicylic acid after clearing the urine of phosphate with acetic acid. The turbidity produced was measured against a reference standard on a spectrophotometer.

The statistical comparison between groups was made using the chi-square test.

Results

Blood pressure values were within normal limits in six patients older than 18 years and in 10 patients younger than 18 years of age. The data of the clearance studies are presented in Table II. The endogenous creatinine clearance values of the patients were slightly but not significantly lower (90.390 ± 11.223 ml/min) than those of control subjects (110.818 ± 7.755 ml/min). The FENa results were not significantly different between the patients with a single kidney and the control subjects ($p > 0.05$).

Table II: The Statistical Comparison of Laboratory Values of Nephrectomized Patients and the Control Group

	Single kidney		Control group			
	Mean	Standard deviation	Mean	Standard deviation	t	p
Ccr (ml/min)	90.390	11.223	110.818	7.755	-1.56	$p > 0.05$
FEna (% mg)	1.292	0.168	1.168	0.135	0.58	$p > 0.05$
TRP (% mg)	84.725	2.357	95.476	0.600	-5.77	$p < 0.001$
Cosm (ml/min)	2.268	0.232	3.188	0.261	-2.54	$p < 0.05$
Prot/Cr (urine)	0.601	0.115	0.285	0.042	3.10	$p < 0.01$
NAG/Cr (U/mmol)	238.433	45.125	133.157	21.537	2.40	$p < 0.05$

The mean phosphorus clearance value in patients with a single kidney was 11.150 ± 1.413, which was significantly higher that of the healthy control subjects (4.774 ± 0.646) (t: 4.67, $p < 0.001$).

Tubular reabsorption of phosphorus was also significantly different from control values (95.476 ± 0.600) in the patients with a single kidney (84.725 ± 2.357) (t: -5.77, $p < 0.001$). The mean osmolar clearance (Cosm) of the patients with one kidney was significantly lower than that of control subjects ($p < 0.05$). The free water clearance of the patients was -1.313 ± 0.208, which was significantly different from that of the control group ($p < 0.001$).

There was also a significant difference in daily protein excretion adjusted for body surface area between the two groups ($p < 0.05$). The ratio of urinary protein to urinary creatinine excretion also differed significantly between the two groups ($p < 0.01$). The mean value of NAG/Cr was 238.433 ± 133.157 in the study group, which was significantly higher than that of the control subjects ($p < 0.05$, Table II).

Discussion

Nephrectomy is performed under various conditions, even in childhood. Urologists and nephrologists routinely reassure patients that a single kidney is sufficient to meet the metabolic demands of the body without development of proteinuria, hypertension and renal insufficiency. However, clinical reports have documented development of proteinuria and hypertension as a result of focal glomerulosclerosis in renal transplant donors[3,4,11].

Terry Watnick et al.[1] found a higher prevalence of hypertension in donors (62%) compared with the expected prevalence adjusted for age, sex and race (42%). The prevalence of hypertension was reported to be higher in male donors as compared to pre-uninephrectomy values and to age-and sex-matched inpatient and outpatient control subjects. Renotropins, which were circulating factors detected in the nephrectomized patients, were suggested to be responsible for the development of hypertension[11].

Ingrid Wikstad et al.[12] studied renal functions and did not find hypertension in their group of patients who had been nephrectomized in childhood. Similar to that study, blood pressure measurements were within normal limits in all of our patients. Perhaps the high prevalence of hypertension among donor nephrectomy patients was due to their ages, as it is known that the incidence of hypertension increases with age. If the follow-up period of our group is longer [7.1 years (1-26)] the incidence of hypertension could be higher.

In most studies the creatinine clearance of the nephrectomized paitents has been within normal limits. In our patient group, the mean creatinine clearance was 81 percent of the control group, but the difference was not statistically significant as it was stated in the literature[13-16].

Following nephrectomy all parts of the nephron enlarge in compensatory hypertrophy; thus, changes involve not only the glomerulus but also the tubulus.

Reabsorbing and secreting salts and water, and concentrating and diluting the urine to maintain homeostasis of the body are the functions of the tubulus. Sodium, bicarbonate, phosphate, amino acids and glucose are reabsorbed primarily by the proximal tubule. In our patient group, while FENa values were normal, Cp and TRP, which show early pathologic changes in the proximal tubulus, were deteriorated; when compared with the control group, the differences were statistically significant.

Proteinuria, which is an early sign of the increase in glomerular permeability, has been detected in nephrectomized patients, and the rate of proteinuria correlates well with the duration of the postnephrectomy period[11, 14]. It has been noted that protein excretion in urine is not albumin, but the source of proteinuria is the impaired absorption of the tubular surface[12, 17]. To prove this, Tapson et al.[8] studied four enzymes [alanine aminopeptidase (AAP), alkaline phosphatase (Akp), NAG and LDH] with high molecular weights that would not permit urine to pass by way of glomerular filtration. If the high concentrations of these enzymes were detected in urine, increased metabolism of the proximal tubulus cells and the defective function of tubular reabsorption could be responsible for the protein excretion.

For this reason we determined NAG in urine, as it has a high molecular weight that cannot be filtrated through the glomerulus. Increased urinary NAG activities indicate renal tubular damage and reflect the activity of the disease[8, 19, 20]. In chronic renal disease, urinary tract obstruction, nephrotic syndrome, glomerulonephritis, rejection of the transplanted kidney, and renal tubular disorders due to the use of aminoglycosides, increased NAG activity in urine has been detected. In our study, statistically significantly high levels of NAG adjusted for Cr values pointed out the increased metabolism of proximal tubulus epithelial cells.

The mean value of NAG/Cr in the study group was significantly higher than that of control subjects. Given the similar results documented in the literature, we concluded that this can be accepted as an indicator of renal tubular damage, as previously suggested by Kunin et al.[5] the presence of normal Ccr values, significant proteinuria and high NAG/Cr values could be interpreted as deterioration in proximal tubular functions.

In summary, we evaluated 16 patients an average of 7.1 years following unilateral nephrectomy or with unilateral agenesis, we concluded that the expected deterioration in renal function, which we detected earlier than reported in the literature, suggests that the defect is mainly at the tubular level, and NAG could be used as an indicator of proximal tubular damage.

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