Renal Clearance of Endogenous Creatinine, Urea, Sodium, and Potassium in Normal Cats and Cats with Chronic Renal Failure

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ABSTRACT. The renal clearance test was carried out in 6 normal male cats and 12 male cats with chronic renal failure. The average concentrations of creatinine (Cr), urea, sodium (Na), and potassium (K) in the serum of the cats with chronic renal failure were 5.09, 136.7 (mg/100 m*l*), 143.9 and 3.71 (mEq/*l*) respectively, and the specific gravity of urine was 1.009. The renal clearances of Cr, urea , Na, and K (m*l*/min/kg of body weight) were 2.639 ± 0.217, 1.034 ± 0.110, 0.024 ± 0.007 and 0.266 ± 0.028, respectively in normal cats, and were 0.789 ± 0.407, 0.358 ± 0.211, 0.095 ± 0.084 and 0.872 ± 0.204 in cats with chronic renal failure. Clearance of Cr and urea was significantly lower in cats with chronic renal failure than in normal cats, while the values of Na and K were significantly higher in cats with chronic renal failure. The glomerular filtration of Cr and urea and the urinary excretion of these 4 substances were significantly higher in cats with chronic renal failure. The tubular reabsorption rates of Na and K were significantly lower in cats with chronic renal failure compared to those in normal cats, but there was no significant difference in urea and creatinine. — KEY WORDS:, chronic renal failure, feline renal clearance test.

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In the literature on feline renal functions, there are reports on feline kidney diseases [1, 2, 17] and hyperthyroidism [12] that were experimentally induced using drugs, and hormone [13, 20] and drug [18, 21, 23] actions, while reports on cats with spontaneous renal failure are few.

With a view to clarifying the renal functions of the cats with chronic renal failure, we carried out a renal clearance test on endogenous creatinine, urea, sodium (Na) and potassium (K), and compared the results obtained with those of the normal cats.

MATERIALS AND METHODS

Six normal male cats, weighing 3.75 ± 0.24 kg (mean ± SD) and 2.0 ± 0.61 years old and 12 male cats with renal disease, weighing 3.4 ± 0.4 kg and 7.4 ± 2.6 years old were used.

On the first medical examination of cats with chronic renal failure, the red blood cell count was 716 ± 206 ($\times 10^4/\mu l$), the leukocyte count was 246 ± 187 ($\times 10^2/\mu l$), and packed cell volume was 31.8 ± 5.2%. Leukocytosis due to neutrophilia and anemia were observed. Blood serum creatinine (BSCr) and blood serum urea nitrogen (BSUN) concentrations were as high as 2.56–8.02 mg/100 m*l* and 65.4–223.5 mg/100 m*l*, respectively, and the chief signs were polydipsia, polyuria, emaciation and dehydration, and in all the cases, the symptoms of uremia such as frequent vomiting and anorexia were observed. The urine specific gravity (SG) was as low as 1.002–1.015, and increased urine SG was not observed in spite of the subcutaneous injection 5–10 units/cat of arginine-vasopressin, proving the nephrogenic diabetes insipidus. The concentrations of blood serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were found to be rather high.

The renal clearance test was carried out during a 60-min period. The urinary bladder was completely emptied with a catheter. After 30 min, approximately 5 m*l* of blood was collected from the jugular vein. When additional 30 min had passed, urine retained in the urinary bladder was completely collected and the volume was measured.

The blood was centrifuged for 15 min at 1,600 × g to obtain the blood serum. The concentrations of urea nitrogen, creatinine (Cr), Na and K in serum and urine were measured by the diacetylmonoximethiosemicarbazide method [4], improved Folin-Wu method [22] and Na-K an autoanalyzer, respectively.

Cr clearance (CCr), urea clearance (Curea), Na clearance (CNa) and K clearance (CK) [mg or mEq/min/kg of body weight (BW)] were obtained by dividing the concentration of each substance excreted into urine per min (mg or mEq/min) by the blood serum concentration (mg or mEq/m*l*) and then by the BW (kg).

For each substance, the following values were calculated: Amount of glomerular filtration (mg or mEq/min/kg of BW) = Serum concentration (mg or mEq/m*l*) × CCr (m*l*/min/kg of BW), Tubular reabsorption rate (%) = [reabsorption by renal tubules (mg or mEq/min/kg of BW) ÷ glomerular filtration (mg or mEq/min/kg of BW)] × 100, where amount of reabsorption by renal tubules (mg or mEq/min/kg of BW) = glomerular filtration (mg or mEq/min/kg of BW) - urinary excretion (mg or mEq/min/kg of BW) .

The significance of differences between means of normal cats and cats with chronic renal failure was tested by the Student's *t*-test.

RESULTS

The results of blood test and urine SG are shown in Table 1. The concentrations of BSCr and BSUN of the cats with chronic renal failure were significantly higher than those of the normal cats ($P<0.001$), while the concentrations of K and urine SG was lower in cats with chronic renal failure ($P<0.01$). However, there was no significant difference in Na between both cases.

The results of the renal clearance tests are shown in Table 2. In normal cats, CCr, Curea, CNa and CK were 2.639 ± 0.217, 1.034 ± 0.110, 0.024 ± 0.007 and 0.266 ± 0.028 (m*l*/min/kg of BW), respectively. On the other hand, the values in cats with chronic renal failure were 0.789 ± 0.407, 0.358 ± 0.211, 0.095 ± 0.084 and 0.872 ± 0.204 (m*l*/min/kg of BW), respectively. CCr and Curea of the cats with chronic renal failure showed a significant decrease compared to those of the normal cats ($P<0.01$), while CNa and CK were significantly higher in cats with chronic renal failure ($P<0.01$).

The results of glomerular filtration, urinary excretion and tubular reabsorption rate of Cr, urea, Na, and K are shown in Table 3. The glomerular filtrations of Cr and urea were higher in cats with chronic renal failure ($P<0.05$), and those of Na and K were higher in normal cats ($P<0.01$). These substances were excreted into urine in amounts 1.5–4.0 times higher in cats with chronic renal failure than those of normal cats ($P<0.01$). The average tubular reabsorption rates (%) of Cr, urea, Na and K of the normal cats were 0, 60.5, 99.1 and 89.9, respectively, and those of the cats with chronic renal failure were 0, 54.1, 87.2 and −56.5, respectively. There was no difference in the tubular reabsorption rate of urea; however, those of Na and K were significantly lower in cats with chronic renal failure compared to the normal cats ($P<0.01$).

Table 1. Blood and urine values in normal cats and cats with chronic renal failure

	Normal cats	Cats with chronic renal failure
Packed cell volume, %	41.3 ± 0.8	31.8 ± 5.2*
Creatinine, mg/100 m*l*	1.01 ± 0.29	5.09 ± 1.82*
Blood urea nitrogen, mgN/100 m*l*	16.5 ± 3.4	136.7 ± 56.8*
Sodium, mEq/*l*	145.7 ± 2.0	143.9 ± 8.3
Potassium, mEq/*l*	4.88 ± 0.12	3.71 ± 0.50*
Urinary specific gravity	1.050 ± 0.009	1.009 ± 0.003*

Values are expressed as mean ± SD.
* $P<0.01$ when compared with values of normal cats.

Table 2. Renal clearance values (m*l*/min/kg of body weight)

Clearance	Normal cats	Cats with chronic renal failure
Creatinine	2.639 ± 0.217	0.789 ± 0.407*
Urea	1.034 ± 0.110	0.358 ± 0.211*
Sodium	0.024 ± 0.007	0.095 ± 0.084*
Potassium	0.266 ± 0.028	0.872 ± 0.204*

Values are expressed as mean ± SD.
* $P<0.01$ when compared with values of normal cats.

Table 3. Glomerular filtration, urinary excretion and tubular reabsorption rate of creatinine, urea, sodium, and potassium in normal cats and cats with chronic renal failure

	Normal cats	Cats with chronic renal failure
Quantity of glomerular filtration		
Creatinine[a)]	0.026 ± 0.006	0.034 ± 0.010
Urea[a)]	0.438 ± 0.109	0.935 ± 0.445*
Sodium[b)]	0.385 ± 0.033	0.115 ± 0.061**
Potassium[b)]	0.013 ± 0.001	0.003 ± 0.002**
Quantity of urine excreted		
Creatinine[a)]	0.026 ± 0.006	0.034 ± 0.010
Urea[a)]	0.169 ± 0.032	0.421 ± 0.195*
Sodium[b)]	0.0035 ± 0.0011	0.0139 ± 0.0125
Potassium[b)]	0.0013 ± 0.0002	0.0032 ± 0.0007**
Tubular reabsorption rate (%)		
Creatinine	0. ± 0	0 ± 0
Urea	60.5 ± 6.1	54.1 ± 9.3
Sodium	99.1 ± 0.2	87.2 ± 8.4**
Potassium	89.9 ± 0.62	–56.5 ± 102.2**

Values are expressed as mean ± SD.
a) mg/min/kg of body weight. b) mEq/min/kg of body weight.
* $P<0.05$ when compared with values of normal cats.
** $P<0.01$ when compared with values of normal cats.

DISCUSSION

Feline diseases of the urinary tract for which we ordinarily have opportunity to treat are feline urological syndrome, urethral obstruction, interstitial nephritis, pyelonephritis, glomerulonephritis and cystic kidney [11, 15]. Interstitial nephritis and pyelonephritis account for a high percentage of feline chronic renal failure cases [5, 7, 8, 11, 15], and are characterized by azotemia, uremia, polydipsia, polyuria, hypokalemia, the decrease in the specific gravity of urine, and dehydration [5, 7, 8, 11, 15, 24]. In the cases which reach an advanced stage, the kidney atrophies and the prognosis is poor [5, 7, 8, 11, 15].

In cats, the blood Cr is filtered by glomeruli in the kidney and excreted into urine without being reabsorbed and reexcreted by renal tubules [10], therefore, CCr represents the glomerular filtration rate (GFR) in cats [10]. In this point, cats differ from dogs where inulin clearance is regarded as the value which represents its GFR [9].

In this experiment, the GFR in the normal cats was 2.639 m*l*/min/kg of BW. This agrees well with 2.51–2.71 m*l*/min/kg of BW in normal cats reported in literatures [12, 19, 21]. Based on GFR of the normal cats in this study, the blood volume to be filtered by glomeruli in 24 hr was estimated to be 9,201 m*l*/kg of BW [(2.639 m*l*/min/kg of BW × 60 min × 24 hr) × 100/41.3 (average PCV)]. As the blood volume of an adult cat was estimated to be 130 m*l*/kg of BW, it was calculated that the total blood volume of a normal cat was filtered by glomeruli 70.8 times in 24 hr (9,201 ÷ 130).

The GFR of the cats with chronic renal failure was 0.789 m*l*/min/kg of BW, which was as low as one third of that of the normal cats. In chronic renal failure, the various uremic toxins, including guanidino derivatives, are formed and accumulated in the body [3, 14, 17] and the symptoms of uremia appear [11, 15], but these uremic toxins cannot effectively be excreted. This seemed to be the reason for the decrease in GFR in cats with chronic renal failure. The concentrations of BSCr and BSUN of the cats with chronic renal failure were 5–8 times higher than those of the normal cats, but the amounts of the glomerular filtration and urinary excretion of these substances increased by only 1.3–2.5 times .

In both the normal cats and the cats with chronic renal failure, it was found that 54.1–60.5% of urea filtered by glomeruli was reabsorbed by renal tubules. This was considered to be the reason that Curea was lower than CCr in both the cats. The Na reabsorption rate of the normal cats was more than 99% but that of the cats with chronic renal failure was as low as 87.2%, and increased urine SG was not observed even when antidiuretic hormone was administered.

From these data, it is clear that the cause of the marked decrease in the urine SG and polyuria observed in cats with chronic renal failure is the decreased water reabsorption due to the lower Na reabsorption by the renal tubules, so, in spite of the symptom of polydipsia, the excretion of water out of the kidney, which was far in excess of the intake of water, expedited the progress of dehydration.

In cats, concentration of blood serum K of 4.1 mEq/*l* or less is called hypokalemia [7, 8], and in the cats with chronic renal failure, it leads to the excessive excretion of K into urine [5, 7, 8]. In this study, the concentration of serum K was 4.1 mEq/*l* or less for 75% (9/12) of the cats with chronic renal failure and the amount of K excreted into urine was larger than that of the normal cats. The reabsorption rate of K by renal tubules was −56.5% for the cats with chronic renal failure in contrast to 89.9% for the normal cats, indicating the increase in the reexcretion rate of K into renal tubules in cats with chronic renal failure. Factors contributing to the development of hypokalemia in cats with chronic renal failure were not fully elucidated, but excessive urinary loss of K combined with the increase of urine volume and the decrease of Na reabsorption rate, i.e., increase of Na into urine observed in this study, were suggested as a possible cause of hypokalemia in cats with chronic renal failure.

In this experiment, the amounts of urinary excretion of Na and K in 24 hr (mEq/kg of BW/day) were calculated to be 5.04 and 1.87 in the normal cats, and 20.02 and 4.64 in cats with chronic renal failure, respectively. The values of Na and K in the normal cats are consistent with those reported by the National Research Council (NRC) [16], but these values in cats with chronic renal failure are higher than those of the NRC [16]. Therefore, it is assumed that the daily requirements of Na and K for the cats with chronic renal failure are 2.5–4 times higher than those for the normal cats. However, it is suggested that the daily requirement of Na for cats with chronic renal failure was the same as that recommended by the NRC for normal cats, and the ratio of K to Na in a diet was 1:2 or higher, since excess Na in a diet leads to hypokalemia in cats with chronic renal failure [6, 7].

In this study, the normal cats were younger in age than the cats with chronic renal failure. Further study is necessary to elucidate the renal function in aged normal cats.

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