The Clearance of Creatinine, Inulin, Para-aminohippurate and Phenosulphothalein in the Cat

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SUMMARY

Endogenous creatinine, inulin, para-aminohippurate and phenolsulphothalein clearances for healthy cats are presented. The values for inulin and para-aminohippurate clearances (ml/kg/min) are similar to those for the dog. Creatinine clearance was less than inulin clearance values. Phenolsulphothalein clearance may be a better index of glomerular rather than tubular function in the cat.

RÉSUMÉ

Les auteurs ont étudié les taux d'élimination chez les chats normaux, de la créatinine, de l'inuline, du para-amino-hippurate et du phénolsulphothaléine endogènes. Ces taux (ml/Kg/min), en ce qui concerne l'inuline et le para-amino-hippurate, sont semblables à ceux du chien. Le taux d'élimination de la créatinine était inférieur à celui de l'inuline. Il est possible que, chez le chat, le taux d'élimination de la phénolsulphotaléine constitue un meilleur indice de l'activité glomérulaire que l'activité tubulaire.

INTRODUCTION

Feline urology has distinct species characteristics. The prominent veins on the cat's kidney capsule are unique but their significance, in terms of renal function, is unknown. The capsule itself is unusual in its lack of smooth muscle fibers (35). All adult cats, except in the anoestrus female (24), have large amounts of intracellular lipids in the proximal tubule as compared with the dog (18, 27). Sodium thiosulphate is actively secreted by the renal tubule cells of the cat's kidney (3, 15) though it is not secreted by kidneys of man, dog and rabbit (3). The daily urine volume (ml/kg bodyweight) voided by a cat (18, 22, 34) is less than that of the dog (12), rat (21) or rabbit (28). The concentration of excreted products in normal cat urine also shows a species difference. Calcium is lower (17) whereas phosphate, creatinine, total solute (17) and magnesium (26) concentrations are higher than in the urine of dog, rat or rabbit. Creatinine excretion is influenced by dietary protein; a low protein and purine free diet is associated with greater daily urinary creatinine excretion (22).

Exogenous rather than endogenous creatinine clearance has been more generally favored in the study of feline glomerular function (2, 13, 16, 14). Eggleton and Habib (14, 16) reported less variability in exogenous creatinine than inulin clearance. Creatinine clearance in the heart-lung-kidney preparations are very much lower than those in the intact animal (10, 25). Although the absolute values were low, the creatinine clearances of the isolated cat kidney were particularly labile.

Published values for PAH clearance in both intact and isolated kidneys vary much less than simultaneous creatinine clearances. Sympathetic stimulation produced by occlusion of the carotid arteries produces little change in renal (7) or hepatic (20) plasma flow. In contrast, the isolated kidney is very sensitive, so renal blood flow alters in response to various stimuli. A single injection or infusion of saline (25) or injection of 2.5 μg aldosterone (10) increases renal blood flow, suggesting that autoregulation in the cat kidney depends at least partially on an intact nervous supply.

It is surprising, therefore, that normal renal function in cats has not attracted more attention. This paper reports the clearance of endogenous creatinine, inulin, para-aminohippurate (PAH) and phenolsulphothalein (PSP) by healthy cats. The values for inulin and PAH clearances (ml/kg/min) are similar to those reported for other small animal species.

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TABLE I. Creatinine, Inulin and Para-aminohippurate Clearances in Nine Cats

Cat #	Hematocrit % cells	Urine Volume ml/min	#20 min periods	cCr ml/min	cIN ml/min	cPAH ml/min	Filtration Fraction
1	45	0.010	6	8.32	13.80	47.4	0.29
2	42	0.0095	8	8.75	9.55	43.4	0.22
3	31	0.053	8	7.85	20.35	41.6	0.48
4	49	0.125	8	13.50	13.55	55.4	0.24
5	50	0.083	4	7.03	9.90	30.4	0.31
6	41	0.247	5	3.46	9.70	62.3	0.15
7	52	0.035	8	7.35	14.1	45.6	0.30
8	42	0.060	5	6.28	10.0	53.4	0.18
9	48	0.150	4	14.79	11.08	48.2	0.22

MATERIALS AND METHODS

The experiments were carried out on 35 anesthetized cats. The animals had been fed a standard ration[1] for at least three days before the experiment, but had not for four hours or longer prior to being anesthetized.

The selected animals were given a preanesthetic medication of 0.3mg propriomazine hydrochloride[2] intravenously. The cephalic vein was cannulated with the cats tranquilized and anesthetic[3] administered intravenously to affect. Then the jugular vein and femoral artery were cannulated with 90 gauge polyethylene tubing, and the urethra cannulated with 160 gauge tubing. The animal was heparinized. An attempt to study the renal function in individual kidneys was made. Each ureter was cannulated with 90 gauge polyethylene tubing but following this procedure urine flow was extremely erratic and therefore unreliable for estimating clearance.

A priming injection of 30 mg/kg bodyweight of inulin and 3 mg/kg of sodium para-aminohippurate was given through the indwelling intravenous polyethylene cannula, and was followed by continuous infusion of 0.2 to 0.4 ml/min of normal saline containing inulin and PAH to produce concentrations of about 20 mg inulin and 3 mg PAH per 100 ml plasma. Criteria for selecting experiments reported were the maintenance of a steady concentration of the chemicals used and normal or near normal urine flow rates. The urine collection periods were 20 minutes duration.

In investigations of the excretion of PSP, normal saline was infused at a rate of 0.5 ml/min via an intravenous cannula; after urine flow rate had become steady, 3 mg of PSP was injected intravenously via the cannula. Ten minute urine collections were made.

At the midpoint of each period 0.5 to 1.0 ml blood was collected. Urine and blood samples were analyzed using microprocedures for inulin (30), PAH (5), creatinine (4) or PSP (32). Clearances of creatinine, inulin, and PAH were calculated in the normal way. PSP clearance was determined by dividing the volume of distribution of PSP by disappearance rate of PSP from the plasma. Urinary PSP concentration was measured at 1:60 dilution.

RESULTS

Creatinine, Inulin and PAH Clearance

Table I shows the results from experiments with constant plasma inulin concentrations less than 40 mg/100 ml, and PAH concentrations less than 3 mg/100 ml. In all but one experiment the inulin clearance exceeded that of creatinine. The mean and standard deviation for inulin clearance, 3.83 ± 0.83 ml/kg/min, was significantly greater ($P < 0.05$) than the creatinine clearance, 2.70 ± 1.12 ml/kg/min. Creatinine clearance was not related to inulin clearance ($r = +.102$), or to plasma creatinine concentration ($r = +0.16$). Mean PAH clearance was 15.1 ±3.48 ml/kg/min and average filtration fraction was 0.21 ranging 0.15 to 0.48. The cat with the lowest filtration fraction had the highest PAH clearance and also the largest urine volume. Data from all cats showed clearance values and urine volumes were unrelated.

[1]C. D. Morris Animal Food, Topeka, Kansas.
[2]Tranvet, Diamond Laboratories, Des Moines, Iowa.
[3]Surital, Eli Lilly & Company, Indianapolis, Indiana.

TABLE II. Percent of Total Urinary PSP Appearing at Ten Minute Intervals Following Intravenous Injection of 3 mg PSP in Seven Cats

Time following injection (minutes)	Percent PSP ± S.D.
0 — 10	11.15 ± 7.3
10 — 20	40.7 ± 13.1
20 — 30	17.4 ± 5.7
30 — 40	10.3 ± 4.2
40 — 50	6.8 ± 2.4
50 — 60	4.7 ± 1.7
60 — 70	3.7 ± 1.9
70 — 80	2.2 ± 2.0
80 — 90	1.7 ± 1.6
90 — 100	1.1 ± 1.4

PSP CLEARANCE

PSP appeared in the urine between three to four minutes after injection. Table II shows the percentage of the PSP injected appearing in the urine at ten minute intervals; all cats had excreted at least 60 percent of the injected dose within 30 minutes. The plasma clearance of PSP (Table III) ranged from 11.8 to 33.8 ml/min. The mean and standard deviation for PSP clearance were 6.3 ± 1.95 ml/kg/min; corresponding values for creatinine clearance were 2.93 ± 0.86 ml/kg/min. Inulin and PAH clearances were not measured simultaneously with PSP clearance. PSP clearance was significantly greater than the creatinine clearance ($P<0.01$).

DISCUSSION

The results suggest that inulin and PAH clearance by the cat, when adjusted to values per unit bodyweight, do not differ from those of the dog (1). The filtration fraction was of similar magnitude to the dog (1), but much greater than that of the rat (11) and rabbit (6).

Normal urine volume for a cat is of the order of 80-100 ml/day (33, 34). When our values for urine flow rate are converted to twenty-four hour urine output, the volume is similar to that of the conscious animal. Anesthesia, therefore, had no undesirable effect on urine production.

The endogenous creatinine clearances (Table I) are not as high as exogenous clearances reported by other workers. One possible explanation is the analytical procedure for estimating urine creatinine. Worden *et al* (34) have pointed out the difficulty of determining creatinine and

TABLE III. Phenolsulphathalein Clearance in Cats

Cat #	Hematocrit % cells	Urine Volume ml/min	^{c}PSP ml/min	^{c}Cr ml/min
1	35	0.22	12.21	6.51
2	36	0.30	26.00	11.44
3	28	0.29	33.81	14.69
4	32	0.17	11.75	6.50
5	33	0.11	19.60	10.30
6	31	0.24	30.82	13.24
7	24	0.06	23.36	14.52

creatine in cat urine. In these experiments all urines were diluted with 5% tungstic acid because subsequent color development was more intense and gave consistent, reproducible creatinine estimates. When water was the diluent, reproducibility was not consistent.

Coles (8) has pointed out that although the PSP urine excretion has distinct limitations, it remains the most practical method for determining tubular function in animals. That is particularly true for the cat because it will void within a few minutes after Urecholine[4] administration. Our results suggest that a 30 minute excretion time with more than 50 percent of the injected dose being excreted would be a satisfactory level for normal function. An advantage of the plasma half time procedure is that the initial dose does not need to be accurately measured. The longest half time in our series was 17 minutes, mean and standard deviation 10.3 ± 2.4 min. With other dye excretion procedures being based on plasma half time (9), this interpretation may become the more popular clinically.

PSP is excreted by both filtration and tubular secretion in dog (31) and man (19), with the greater proportion of the dye being excreted by tubular activity. The capacity to secrete PSP is much more highly developed in man than in the dog. The PSP to inulin clearance ratio in man is 3.2 as compared with 1.75 in dog. Simultaneous inulin and PSP clearances were not performed in this series of experiments; the ratio derived from PSP and the inulin clearance in Tables I and II was 1.5 indicating the cat is similar to dog in its capacity to secrete PSP.

[4]Merck and Company, Rahway, New Jersey.

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