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## Short-term hemodialysis treatment in dogs and cats with total uretic obstruction

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### Abstract

This study evaluated the single-pass system for the short-term dialysis treatment of dogs and cats with experimental renal failure. The hemodialyzer was equipped with a thin and highly permeable Cuprophane membrane. Four animals (two dogs and two cats) with total uretic obstruction were dialyzed twice in a one-week period. The vascular access by venipuncture of external jugular vein delivered more than 5 ml/min/kg/body weight of blood repeatedly, even for the cats. The evaluation of the effects of the blood flow, dialysate flow and ultrafiltration pressure revealed that the blood flow was the most important factor for effective dialysis. A 300 ml/min dialysate flow provided enough clearance of blood urea nitrogen and creatinine. The ultrafiltration pressure played an important role in ensuring that the fluid removal was constant. Laboratory studies revealed a 50.0% (range 42.0 to 59.3%) reduction of blood urea nitrogen, a 48.7% (range 42.5 to 58.7%) reduction of creatinine, and a 49.8% (range 34.3 to 66.2%) reduction of inorganic phosphate during the dialysis treatment. No dialysis disequilibrium syndrome was shown by the clinical signs. We conclude that this short-term dialysis using a single-pass system for small animals was sufficiently applicable to dogs and cats, and that the optimal duration of the dialysis was 2 hours.

Key words : Hemodialysis, Dog, Cat, Short dialysis, Blood flow

### Introduction

Though applications of hemodialysis in dogs have been described since 1968, hemodialysis is not often used in veterinary medicine, in contrast to its application in human medicine<sup>4,20</sup>. The clinical studies describe the use of hemodialysis in dogs with acute<sup>8,9</sup> or chronic renal failure<sup>1,18</sup>, and the vascular access and anticoagulation<sup>19</sup> and ultrafiltration and infusion rates<sup>10</sup>. In Japan, however, animal hemodialysis therapy is limited at present to some of the university veterinary

teaching hospitals because of the need for specialized technical personnel, versatile clinical laboratory procedures and intensive care facilities, and economic considerations. Hemodialysis equipment for small animals has been available in Japan for several years. This simple equipment controls only the extracorporeal flows of blood and dialysate and the temperature of the dialysate, and monitors the arterial pressure. The dose of heparin, ultrafiltration pressure (UFP), and correction of fluid overload must be regulated independently. This equipment also adopted 10

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liters of a dialysate bath and a dialysate recirculation system.

In the present study, we modified the dialysate recirculation system to a single-pass system (SPS) to investigate short-term dialysis treatment for dogs and cats.

### Materials and Methods

The hemodialyzers for small animals were of hollow fiber design and composed of Cuprophane membranes. All of the equipment was produced by Senko Medical Instrument Manufacturing Co. (Tokyo, Japan). Two membrane characters were used: thin and highly permeable (H), and thick and less-permeable (L). Two surface areas were used for these membranes: 0.2 and 0.5m<sup>2</sup> denoted as 0.2H, 0.5H and 0.2L, 0.5L, respectively. The dialysis delivery system was a modified SPS, which was composed of the regulators of the dialysate flow and the temperature. An accumulator which regulates the UFP was connected to the blood lines. An infusion pump was also connected for precise ultrafiltration and fluid removal. The anticoagulant was administered to the outflow side of the blood line according to a previously described method<sup>19</sup>. Sixty units of heparin per kg of body weight (BW) were administered at the beginning of the dialy-

sis, and thereafter, 60 units/kg/BW of heparin were administered continuously each hour. A dialysate tank which holds up to 200 l of dialysate (Kindaly solution AF2, FUSO Pharmaceutical Industries, Co., Osaka, Japan) was used (Fig. 1). The blood line and hemodialyzer were thoroughly rinsed and primed with the heparinized saline (10 units of heparin in one ml).

Healthy bovine blood was dialyzed for the evaluation of the following dialysis factors: dialysate flow (QD), blood flow (QB), the membrane of the hemodialyzer, and the UFP. Five grams of urea and 0.15g of creatinine powder (Wako Pure Chemical Industries, Co., Osaka, Japan) were added to each liter of blood, which was then heparinized by 5,000 units of heparin sodium. To determine the optimal QD, the bovine blood was dialyzed at the QD rates of 150, 200, 250, 300, 400 and 500 ml/min. The 0.2H dialyzer was used and the QB rate of 40 ml/min was kept constant. The clearances of the 0.5H and 0.5L dialyzers were compared under variable condition of QB; 40, 50, 60, or 70 ml/min. The effect of the QB was evaluated at the same time. The effect of the UFP was evaluated using bovine blood with the 0.2H dialyzer. The QB was maintained at 20, 30, 40 or 50 ml/min. The UFP was changed from natural pressure to 200, 300

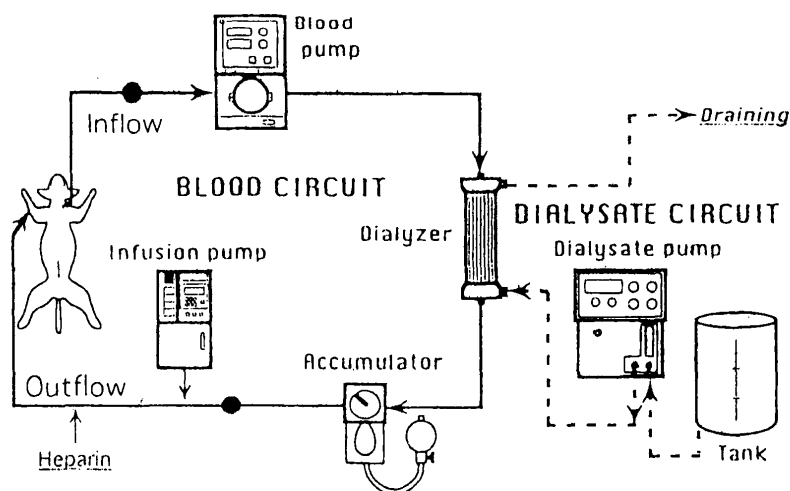


Fig. 1. Schematic representation of the hemodialysis circuit.

●: Sampling points for inflow and outflow sides.

and 400 mmHg.

Two beagle dogs and two mongrel cats were prepared as follows: the bilateral distal ureters were ligated with nylon sutures, and the animals were administered saline containing 20% glucose, H<sub>2</sub> blocker, metoclopramide and antibiotics during the experimental period. The animals with acute uremia were dialyzed by the following methods; the sizes of the dialyzer (0.05H, 0.1H, 0.5H and 0.8H) were chosen in accordance with the body size of the animal. Hemodialysis was done on the 3rd and 5th day after the ligation. The animals were premedicated by atropine and anesthetized by isoflurane. For the dogs, a 19-gauge intravenous catheter with side holes (Happy-cath, Medikit Co., Tokyo, Japan) was inserted into an external jugular vein to obtain blood, and an 18-gauge intravenous catheter (Insyte-W, Nippon Becton Dickinson Co., Tokyo, Japan) was placed in the cephalic vein to return blood. For the cats, a 20-gauge Insyte-W catheter was used to return blood. At the end of the hemodialysis treatment, protamine sulfate was administered according to the previously reported method<sup>19</sup>. The potassium in the dialysate was adjusted within the range from 2.0 to 4.0 mEq/l, and the QD in every treatment was kept at 300ml/min.

The concentrations of blood urea nitrogen (BUN), creatinine (Cre), and inorganic phosphate (iP) were measured by an automated blood chemistry analyzer (COBAS MIRA S: Nippon Roche Co., Tokyo, Japan). Plasma sodium, potassium, and chloride concentrations were measured by a dry chemistry system (Fuji Drychem 800: Fuji Medical System, Co., Tokyo, Japan). The results are presented as the reduction ratios for a two-hour period. The clearances of BUN and Cre were determined by the following formula<sup>16</sup>:

$$CL = \frac{C_{in} - C_{out}}{C_{in}} QB + \frac{C_{out}}{C_{in}} QF$$

Where CL is the clearance of each substance

(ml/min), QB is the blood flow rate (ml/min), C<sub>in</sub> is the serum concentration of the inflow side (mg/dl), C<sub>out</sub> is the serum concentration of the outflow side (mg/dl) and QF is the quantity of the filtrate (ml/min). The packed cell volume (PCV) and concentrations of total plasma protein were also measured during the dialysis. Pearson's statistical analysis was utilized in order to find linear combinations of the variables.

### Results

The changes of CL-BUN and CL-Cre under various conditions of QD in bovine blood are illustrated in Fig. 2. Both of these clearance values in the SPS were increased steeply (from 31.8 and 23.9 to 33.8 and 31.8, respectively) below the QD of 300 ml/min, and increased slightly (to 34.7 and 33.2, respectively) at the QD of 300 ml/min.

A linear relationship was observed between the clearance of the dialyzer membrane and the QB (Fig. 3). The regression lines obtained in the experiments with a highly permeable membrane were BUN:  $y = 0.67x + 12.0$  ( $r = 0.998$ )

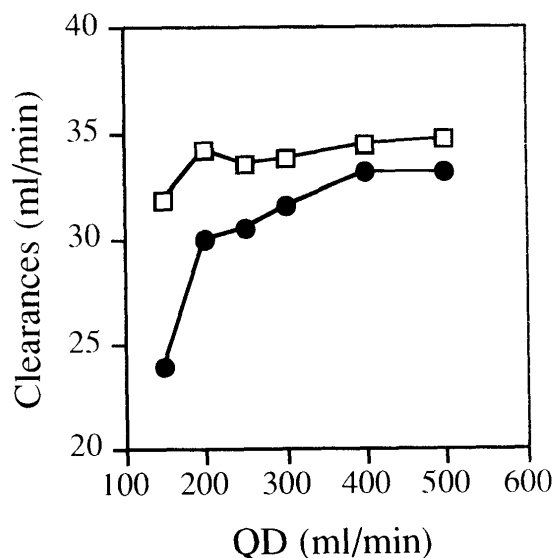


Fig. 2. The effect of dialysate flow on the clearances of BUN and Cre.

(Dialyzer: 0.2H, QB: 40 ml/min)

□: BUN      ●: Cre

and Cre:  $y=0.63x+6.8$  ( $r=0.992$ ). Those with a lower permeable membrane were BUN:  $y=0.27x+32.4$  ( $r=0.995$ ) and Cre:  $y=0.24x+30.2$  ( $r=0.990$ ).

The effects of UFP on CL-BUN and CL-Cre were not clear, and linear relationships were not obtained at any QB in the 0.2H dialyzer. When the QB was kept at 30 ml/min, the BUN clearance increased by 5.5%, with a 200 mmHg increase of

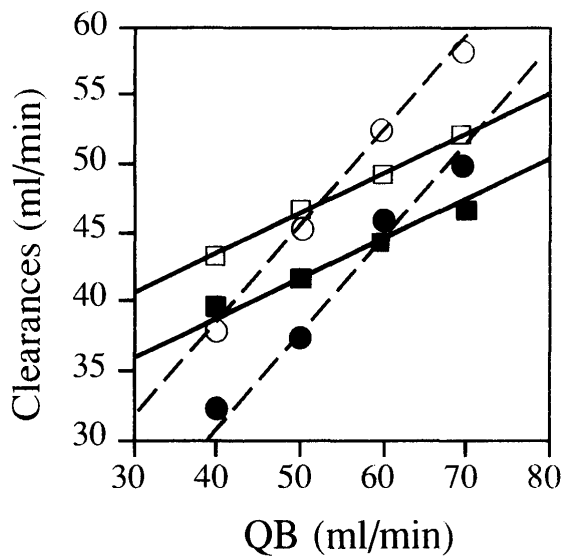


Fig. 3. The relationship between the BUN and Cre clearances and blood flow (QB) with different membrane permeabilities.

(Dialyzer: 0.5L and 0.5H, QD: 300 ml/min)

□: BUN (0.5L)  $y=0.27x+32.4$

■: Cre (0.5L)  $y=0.24x+30.2$

○: BUN (0.5H)  $y=0.67x+12.0$

●: Cre (0.5H)  $y=0.63x+6.8$

UFP. When the QB was adjusted to 40 and 50 ml/min, the increases were by 24.1 and 1.3%, respectively (Fig. 4). Each of the values mentioned above was obtained with a single experiment.

The dialysis conditions of the four experimental animals are listed in Table 1. The QB was kept in the range from 3.75 ml/min/kg to 5.8 ml/min/kg in all cases (15 to 80 ml/min). The QB of 60 ml/min and 15 ml/min was easily

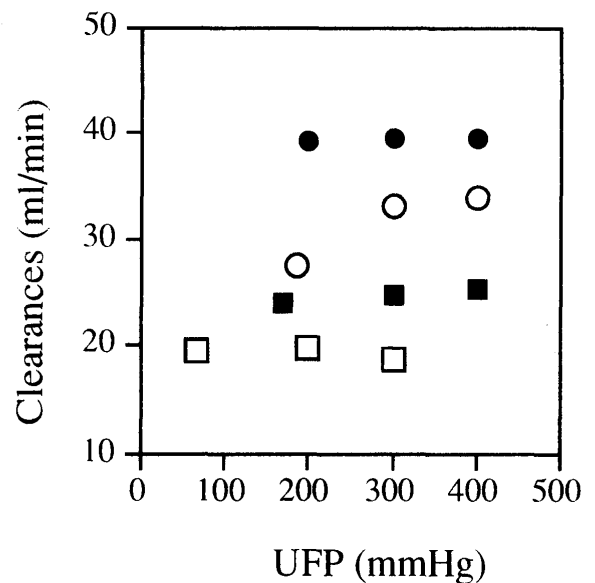


Fig. 4. The relationship between the ultrafiltration pressure (UFP) and BUN clearances under the various blood flow (QB) conditions.

(Dialyzer: 0.2H, QD: 300 ml/min)

□: QB=20    ■: QB=30

○: QB=40    ●: QB=50

Table 1. The in vivo hemodialysis conditions for each animal.

Animals (kg)	Treatment	Dialyzer	QB <sup>a)</sup> (ml/min)	UFP <sup>b)</sup> (mmHg)	Time <sup>c)</sup> (min)
Dog 1 (16 kg)	1st	0.8 H	80	300	120
	2nd	0.5 H	60	300	120
Dog 2 (14 kg)	1st	0.8 H	70	280	120
	2nd	0.8 H	70	280	120
Cat 1 (3.4 kg)	1st	0.05H	15	250	120
	2nd	0.1 H	20	250	120
Cat 2 (3.6 kg)	1st	0.05H	20	300	120
	2nd	0.1 H	20	300	120

a) QB: blood flow rate.

b) UFP: ultrafiltration pressure.

c) Time: the duration of hemodialysis.

Table 2. Dialysis treatment results.

Animal	Treatment		Serum concentration (mg / dl)			Reduction rate (%)		
			BUN	Cre	iP	Bun	Cre	iP
Dog 1	1st	Pre	118.9	7.8	18.2	51.1	48.7	48.4
		Post	58.1	4.0	9.4			
Dog 1	2nd	Pre	142.7	6.2	17.1	42.0	43.5	34.3
		Post	82.8	3.5	11.9			
Dog 2	1st	Pre	172.5	5.7	43.8	47.7	49.1	66.2
		Post	90.3	2.9	14.8			
Dog 2	2nd	Pre	138.9	4.9	27.2	59.3	51.0	58.1
		Post	56.6	2.4	11.4			
Cat 1	1st	Pre	85.8	5.6	9.6	42.7	41.1	34.4
		Post	49.2	3.3	6.3			
Cat 1	2nd	Pre	115.4	6.3	10.4	52.8	58.7	48.5
		Post	54.5	2.6	5.5			
Cat 2	1st	Pre	145.3	11.3	14.9	48.7	42.5	51.0
		Post	74.5	6.5	7.3			
Cat 2	2nd	Pre	140.0	13.4	21.4	55.9	55.2	57.5
		Post	61.7	6.0	9.1			

obtained in the dogs and cats, respectively. Table 2 shows the serum concentrations of BUN, Cre, and iP pre- and post-dialysis, and each reduction rate before and after the hemodialysis in the dogs and cats. When the SPS equipped with a dialyzer with a permeable membrane and accumulator was used in these uremic animals, the mean reduction rate of BUN obtained was 50.0% (range 42.0 to 59.3), that of Cre was 48.1% (range 43.5 to 51.0), and that of iP was 51.8% (range 34.3 to 66.2) within two hours for the dogs. For the cats, the comparable figures were 50.0% (range 42.7 to 55.9) for mean BUN, 49.4% (range 41.1 to 58.7) for Cre, and 47.9% (range 34.4 to 57.5) for iP. Clinical signs such as vomiting and diarrhea did not worsen after the treatment in any animals, although a remarkable recovery was not observed. The recovery from anesthesia was uneventful in every case.

### Discussion

The dialysis delivery systems used for humans control or monitor the following parameters: the amount of dialysate, the composition, temperature and pH of the final fluid, the

extracorporeal flow of blood, the rate of ultrafiltration, and the delivery of heparin. The same type of computerized system has been used in veterinary medicine in the United States<sup>5,6</sup>, while only a recirculation system has been used clinically in veterinary medicine in Japan. This recirculation system controls only the extracorporeal flows of the blood and dialysate and the temperature of dialysate, and monitors the arterial pressure. Other factors must be controlled by the clinicians. This system contains only 10 liters of dialysate bath, and uses a dialysate recirculation system. The present study was designed to establish short-term dialysis treatments for dogs and cats using an SPS with a modified the recirculation system, combined with a non-computerized system.

Our results suggested that a QD of 300 ml/min was sufficient to obtain enough clearances of BUN and Cre. The clearances obtained by using a highly permeable membrane were more increased than those using a less permeable membrane within a range of higher QB. When a higher QB cannot be obtained, the dialyzer with a smaller surface area should be used. The QB

was the more effective factor for the dialysis compared with the QD, and the effect of the UFP on the BUN and Cre clearances was very small. However, the accumulation of the UFP plays important roles both in the removal of serum middle-sized molecules<sup>12)</sup> and in keeping the fluid removal constant<sup>10)</sup>. Previous studies found that the reduction of serum middle-sized molecules influences the clinical result of dialysis treatment<sup>3,22)</sup>. The reason that the middle-sized dialyzers such as 0.2 and 0.5H were used in vitro studies was that clotting or stagnation would be generally observed in smaller- or larger-sized dialyzers.

An adequate blood flow was obtained by the venipuncture of the external jugular vein in the present study, while single-<sup>1,14)</sup> and double-lumen catheters<sup>5,6)</sup> and arteriovenous shunts<sup>9)</sup> were used in previous investigations. We found that the reduction ratios of both BUN and Cre were more than 50% within two hours of dialysis. It took 3 to 4 hours to get the same results using a recirculation system<sup>18,19)</sup>. What is most important is how this high-efficiency hemodialysis affects the animal subjects. The clinical signs of these dialyzed animals were not worsened by the dialysis treatment in our study. In a previous report, the recirculation system was used for the prevention of the dialysis disequilibrium syndrome<sup>15)</sup>, since too-rapid dialysis results in this syndrome<sup>11,17)</sup>. We found that the short-term hemodialysis in this study did not induce a dialysis disequilibrium. Peritoneal dialysis<sup>2,21)</sup> and hemofiltration<sup>13)</sup> are also effective methods for blood purification in small animals. However, the side effects of these treatments such as protein and amino acid loss and peritonitis<sup>7)</sup> have not been adequately resolved, and the treatments require a long therapy period.

In conclusion, the higher the QB is, the better effect of hemodialysis is obtained. Unfortunately, in small animals, because of their body size, sufficient QB cannot always be obtained

using equipment for human dialysis. However, by using the SPS described herein equipped with a thin and highly permeable membrane plus an accumulator, satisfactory dialysis was achieved. The duration of dialysis was shorter than that needed in the use of the recirculation system, thus reducing the burdens on the subjects caused by restraint and sedation.

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