

## Original Article

# Hematologic and hemodynamic findings during hemodialysis in 13 beagle dogs

Chang-Moo Ji, Hae-Won Jung, Hyo-Mi Jang, Jong-Hyun Moon, Dong-In Jung \*

*Institute of Animal Medicine, College of Veterinary Medicine, Gyeongsang National University, Jinju 660-701, Korea*

**Hemodialysis is an effective therapy for renal failure in veterinary practice. To evaluate hematologic and hemodynamic changes during hemodialysis, 13 dogs were treated with hemodialysis, after which complete blood cell counts (CBC), serum chemistry, and mean systolic blood pressure were analyzed. For CBC, white blood cells (WBC) and platelets underwent significant changes. In serum chemistry, there were significant differences in blood urea nitrogen (BUN), creatinine, total protein, albumin, globulin, amylase, calcium, potassium, and phosphorus contents. Further, mean systolic blood pressure suddenly increased in early hemodialysis and decreased significantly thereafter. During hemodialysis, adverse effects were observed in some dogs as follows: bleeding (1 dog), anemia (2 dogs), leukopenia (8 dogs), thrombocytopenia (2 dogs), and hypotension (1 dog). This study demonstrates hematologic and hemodynamic effects during hemodialysis as well as complications similar to human medicine. Before applying the commercialized human hemodialysis system to canine renal failure patients, we monitored hematologic and hemodynamic findings during hemodialysis in healthy beagle dogs.**

**Key words:** hemodialysis, renal failure, dog

## Introduction

Renal failure occurs when renal functional capacity is impaired, and results in retention of nitrogenous waste products and imbalance of fluid, electrolyte, and acid-base [1]. As a result, renal failure, including acute renal failure (ARF) or chronic kidney disease (CKD), causes considerable mortality and morbidity according to progressing of renal dysfunction. Conventional treatments are focused on fluid therapy for improving azotemia, correction of electrolyte and acid-base abnormalities, and alleviation of clinical signs. However, unless there is no

response to medical therapy in patients with ARF, uremic crisis that the kidneys cannot filtrate urea (body waste) is present and causes blood poisoning. Also, as time passes, traditional treatments of CKD patients will be predictably frustrating as renal function declines.

In these cases, hemodialysis, one of the renal replacement therapies, can be a great alternative in patients with ARF or CKD that is potentially life-threatening. Hemodialysis is the most common procedure of renal replacement therapy for the majority of human patients with severe uremia [2]. In Korea, however, hemodialysis in veterinary practice has been limited by high-priced equipment and hemodialysis-induced complications. Also, there are not so much as studying about complications associated with hematologic and hemodynamic changes during hemodialysis.

Therefore, the purpose of this study is to apply the hemodialysis procedure for more efficiency and to investigate clinical consequences associated with complications of hemodialysis in hematology and hemodynamics.

## Materials and Methods

Thirteen clinically healthy beagles (weighing 8.3 to 16.7 kg) were used in this experiment. Physical examination, CBC, and serum chemistry were performed in all dogs before the hemodialysis procedure. Although there was no imaging test, they were determined to be clinically healthy.

## Hemodialysis procedure

Before the hemodialysis procedure, a catheterization with double lumen catheter kit (GamCath GDK-610K®, GAMBRO, Germany) (Fig. 1B) into external jugular vein was performed after the general anesthesia.

Hemodialysis was performed with dialysis delivery

\*Corresponding author: Dong-In Jung, Institute of Animal Medicine, College of Veterinary Medicine, Gyeongsang National University, Jinju 660-701, Korea  
Tel: +82-55-772-2361, E-mail: jungdi@gnu.ac.kr

system (AK 95 S<sup>®</sup>, Gambro, Sweden) (Fig. 1A) for 120 minutes, using convective and diffusive solute clearance with ultrafiltration. Hollow fiber dialyzers (Polyflux<sup>®</sup> 6H, Gambro Dialysation GmbH, Germany) (Fig. 1C) as an artificial kidney and medical lines (Shanghi line<sup>®</sup>, Gambro medical products, China) as extracorporeal tubing were used. Commercial balanced electrolytes dialysate that baths the blood-filled hollow fibers in the dialyzer was used. HD Sol-BCG<sup>®</sup> (Gambro solution, Korea) and BiCart<sup>®</sup> (Gambro Lundia AB, Sweden) were used as A solution and B solution, respectively. The dialysate was proportioned from A and B solutions and highly purified water to final composition of Na<sup>+</sup>=135 to 140 mEq/L, K<sup>+</sup>=2.5 mEq/L, Ca<sup>2+</sup>=3.5 mEq/L, Mg<sup>2+</sup>=1.5 mEq/L, Cl<sup>-</sup>=106.5 mEq/L, acetic acid=8 mEq/L, and HCO<sub>3</sub><sup>-</sup>=30 to 34 mEq/L. Water was the most abundant component of dialysate and was supplied by water-purified device (WRO 300<sup>®</sup>, Gambro, Sweden).

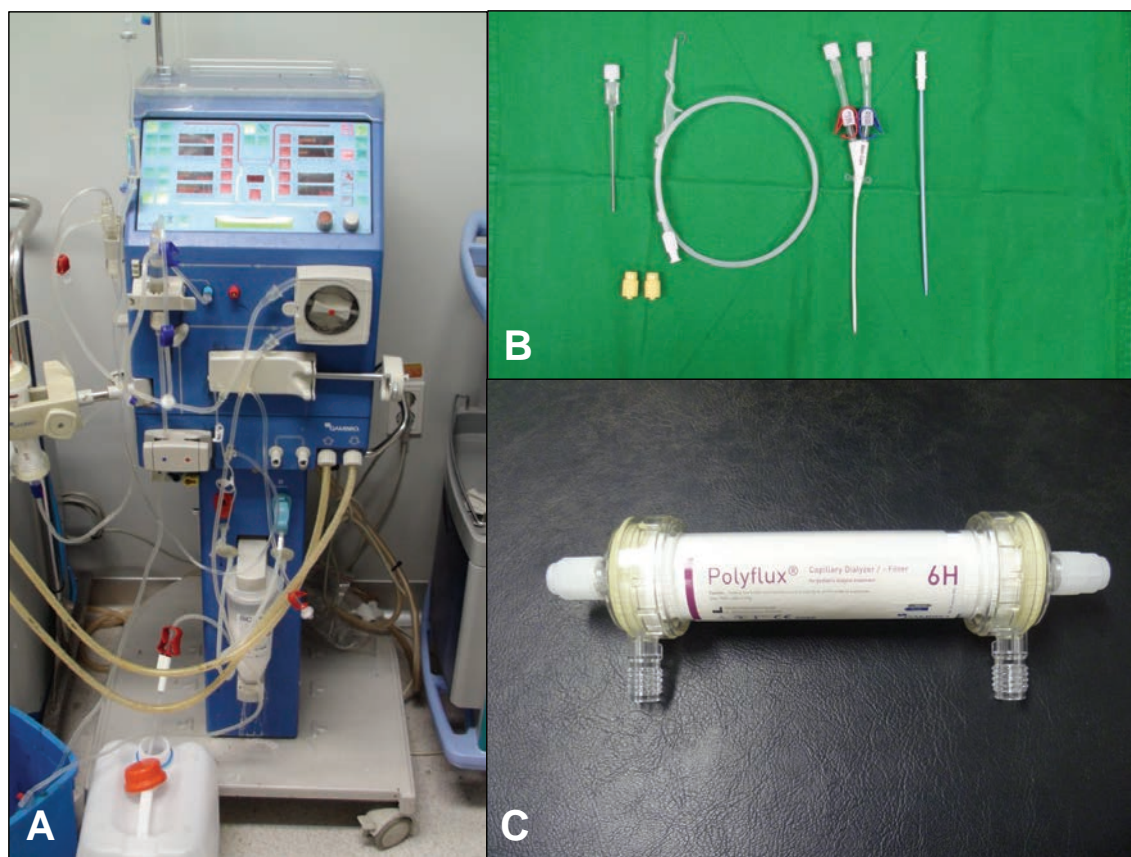
A blood flow rate was restricted to 3 to 5 mL/kg/min to prevent dialysis disequilibrium and increased gradually 8 to 12 mL/kg/min. Also, an anticoagulant treatment was necessary to prevent blood clotting during hemodialysis

because exposure of blood to the dialyzer membrane and the extracorporeal circuit causes coagulation. To prevent blood clotting, heparin was administered as loading dose at 100 unit/kg and was continued as maintaining dose at 1200 unit/kg/hr, intravenously in this study.

To carry out the hemodialysis procedure with same circumstance, all dogs were sedated with medetomidine (Domitor<sup>®</sup>, Pfizer, USA) at dose 40 to 50 µg/kg, intramuscularly. Because its effect persisted for 60 minutes in case of administering intramuscularly, the sedation was accomplished at hemodialysis time 0 and 60 minute, respectively. Atipamezole (Antisedan<sup>®</sup>, Pfizer, USA) was used as a reversal agent (40 to 50 µg/kg, intramuscularly) for medetomidine at hemodialysis time 120 minute.

### Blood profiles and systolic blood pressure

To evaluate hematologic and hemodynamic changes, CBC (MS9-5<sup>®</sup>, MS, France) and serum chemistry (VetScan<sup>®</sup>, Abaxis, USA) were analyzed at hemodialysis time 0, 60 and 120 minutes, and mean systolic blood pressure was measured with oscillometry (CARDELL<sup>®</sup>, Sharn veterinary, USA) at 10-minute intervals during he-



**Fig. 1.** Compositions for hemodialysis in this study. The dialysis delivery system is equipped with extracorporeal circuit, dialysate and hollow fiber dialyzer before hemodialysis (A). The double lumen catheter kit is used for the catheterization and pediatric use in human medicine (B). The hollow fiber dialyzer serves as an artificial kidney and is also used for pediatric use in human medicine (C).

modialysis.

### Statistical analysis

All data were expressed as mean  $\pm$  S.D. and were analyzed by one-way ANOVA. A  $P$ -value  $< 0.05$  was considered statistically significant.

### Results

All 13 hemodialysis procedures were performed for 120 minutes and the influences of hemodialysis were evaluated by CBC, serum chemistry and systolic blood pressure.

#### Blood profiles

In CBC, WBC and platelet showed significant changes. WBC represented  $9.3 \pm 2.66 \times 10^3/\mu\text{L}$ ,  $5.3 \pm 2.21 \times 10^3/\mu\text{L}$  and  $7.3 \pm 2.55 \times 10^3/\mu\text{L}$  at hemodialysis time 0, 60 and 120 minute, respectively. Leukopenia was detected in 8 dogs. Platelet showed  $357.0 \pm 134.5 \text{ m/mm}^3$ ,  $231.3 \pm 103.6 \text{ m/mm}^3$  and  $206.0 \pm 72.4 \text{ m/mm}^3$  at hemodialysis time 0, 60 and 120 minutes. Thrombocytopenia was observed in 2 dogs. However, there was no significant change in PCV.

In serum chemistry, BUN, creatinine, total protein, albumin, globulin, amylase, calcium, potassium and phosphorus represented significant results. Serum titer of BUN, creatinine, potassium and phosphorus laid emphasis on when renal failure occurs were as the follows; Serum BUN decreased from  $14.54 \pm 5.23 \text{ mg/dL}$  to  $7.85 \pm 2.444 \text{ mg/dL}$ . Serum creatinine decreased from  $0.67 \pm 0.144 \text{ mg/dL}$  to  $0.50 \pm 0.158 \text{ mg/dL}$ . Serum phosphorus decreased from  $4.65 \pm 0.788 \text{ mg/dL}$  to  $3.72 \pm 0.743 \text{ mg/dL}$ . In case of potassium, the values at each time were as the follows;  $4.45 \pm 0.546 \text{ mmol/L}$  at hemodialysis time 0 minute,  $3.88 \pm 0.480 \text{ mmol/L}$  at hemodialysis time 60 minute, and  $3.92 \pm 0.616 \text{ mmol/L}$  at hemodialysis time 120 minute.

Total protein decreased from  $6.56 \pm 0.528 \text{ g/dL}$  to  $5.11 \pm 0.908 \text{ g/dL}$ . Serum albumin and globulin decreased from  $3.45 \pm 0.299 \text{ g/dL}$  to  $2.69 \pm 0.470 \text{ g/dL}$ , and from  $3.12 \pm 0.524 \text{ g/dL}$  to  $2.41 \pm 0.665 \text{ g/dL}$ , respectively. Also, amylase decreased from  $686.92 \pm 243.072 \text{ U/L}$  to  $417.15 \pm 178.967 \text{ U/L}$  and serum calcium decreased from  $10.08 \pm 0.462 \text{ mg/dL}$  to  $8.81 \pm 0.812 \text{ mg/dL}$ .

However, no significant differences in sodium, glucose and total bilirubin, ALP, and ALT were showed.

#### Systolic blood pressure

Mean systolic blood pressure before hemodialysis was  $141.4 \pm 18.39 \text{ mm Hg}$ . Systolic blood pressure suddenly increased in early hemodialysis procedure, and thereafter it had a tendency to gradually decline. Hypotension was observed only 1 dog (69 mm Hg) during hemodialysis

although duration of hypotension was temporary.

### Discussion

Traditionally, therapies with renal failure patients are designed to correct abnormalities in fluid, acid-base, electrolyte and nutritional balance to minimize disturbances of renal impairment [3]. Over the years, these therapies have been developed. Hemodialysis, however, in dogs and cats with renal failure is eventually indicated when no conventional therapy would be efficient. Many technical limitations have been overcome thanks to development of devices such as catheter and dialyzer, and newer dialysis delivery system [2]. In this study, 13 dogs are successfully treated for 120 minutes with modern equipment.

Hemodialysis provides many therapeutic advantages. However a lot of complications interfere with the course of hemodialysis [4]. These are hemodynamic (hypotension), and hematologic, respiratory, neurologic and gastrointestinal complications. These complications have been reported with human CRRT [5, 6]. There were a few adverse events in this study, including 1 dog with hypotension, 1 dog with bleeding, 2 dogs with anemia, 8 dogs with leukopenia and 2 dogs with thrombocytopenia.

Hypotension is a common adverse effect during hemodialysis. This is because of large blood volume of extracorporeal circuit, and blood loss secondary to dialyzer or blood line clotting. In this study, hypotension was temporarily observed only 1 dog although volume of extracorporeal circuit and dialyzer (140 mL) applied to all dogs was larger than that of previous report, 113.5 mL and 84 to 107 mL, respectively [5, 7]. Despite hypotension is the common complication during hemodialysis, the reason why hypotension was rarely observed in this study regards as the same amount of priming solution in the extracorporeal circuit then entered the patient when blood was passed from patients to the hemodialysis unit. Additionally, this was probably because duration of hemodialysis (120 minutes) in this study was shorter than median duration in the previous report and the dogs used in this study were clinically normal [5, 7].

Hematologic changes involved with complication are thrombocytopenia, leukopenia, and anemia. This is that neutrophil and platelet become sequestered in the pulmonary capillary [4, 5, 7]. Also, macrophage and monocyte play a main role in this phenomenon. This is because macrophage and monocyte become activated and increase productions of cytokines [4, 5, 7]. This consequence returns to near normal circulating levels approximately 1 hour after the start of hemodialysis. Anemia is associated with blood loss.

In serum chemistry, BUN, creatinine, total protein, albumin, globulin, amylase, calcium, potassium and phos-

phorus represented differences between before and after hemodialysis. However, those differences were within reference ranges and suspected as results of dilution effects of the priming solution and hemodialytic influence.

There are two limitations of this study. One is its small population that limits statistical significance in terms of trends in outcome. For more meaningful outcome, large studies will be necessary to clarify variables that affect consequences. The other is that subjects of this study are clinically healthy dogs. Critically abnormal patient would appear more unstable condition hematologically or hemodynamically than that of healthy patient and potentiality of adverse effects in hemodialysis may increase.

In conclusion, this study demonstrates the hematologic and hemodynamic responses to hemodialysis. Complications in veterinary practice are similar to those in human medicine.

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