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เทคนิคการฟอกเลือดสุนัขที่มีภาวะยูรีเมียเฉียบพลันและภาวะแทรกซ้อน

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บทคัดย่อ: สุนัขพันธุ์ผสมอายุ 8 ปี น้ำหนัก 20 กิโลกรัม มีภาวะโลหิตจาง หายใจลำบากเนื่องมาจากภาวะปอดบวม และภาวะยูรีเมีย (ค่า Blood Urea Nitrogen; BUN = 250 มิลลิกรัมต่อเดซิลิตร ค่า creatinine = 18.4 มิลลิกรัมต่อเดซิลิตร) ไม่พบปัสสาวะมา 3 วัน พิจารณาการฟอกเลือดด้วยเครื่องไตเทียม ณ หน่วยโรคระบบทางเดินปัสสาวะ โรงพยาบาลสัตว์มหาวิทยาลัยเกษตรศาสตร์ วิทยาเขตบางเขน ทำการฟอกเลือดด้วยเครื่องไตเทียมเป็นจำนวน 3 ครั้ง โดยกำหนดอัตราการนำเลือดมากรอง 5มล./กก./นาที 5 มล./กก./นาที และ 6 มล./กก./นาที ตามลำดับ กำหนดอัตราการไหลของน้ำยาฟอกเลือดผ่านตัวกรองคงที่ 500 มม./นาที กำหนดค่ากรองน้ำส่วนเกิน 1.2 ลิตร, 0.4 ลิตร และ 0.7 ลิตร ตามลำดับ กำหนดระยะเวลาในการฟอกเลือด 90 นาที 90 นาที และ 150 นาทีตามลำดับ ผลของการรักษาพบว่าอัตราการลดลงของยูเรียระหว่างการฟอกเลือดแต่ละครั้ง เท่ากับ 0.47 0.45 และ 0.52 ตามลำดับ สัตว์ป่วยใช้ระยะเวลาทั้งหมดในการรักษาภายในโรงพยาบาลสัตว์เป็นเวลา 14 วัน สุนัขสามารถกลับบ้านและใช้ชีวิตประจำวันได้ โดยอยู่ในภาวะไตวายระยะที่ 3 (ค่า BUN = 37 มิลลิกรัมต่อเดซิลิตร ค่า creatinine = 3.2 มิลลิกรัมต่อเดซิลิตร) สุนัขมีชีวิตอยู่นาน 120 วัน ในรายงานสัตว์ป่วยนี้ได้กล่าวถึงรายละเอียดขั้นตอนการฟอกเลือดด้วยเครื่องไตเทียม

คำสำคัญ: ภาวะไตวาย ภาวะยูรีเมีย การฟอกเลือดด้วยเครื่องไตเทียม

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Technique of Hemodialysis in Acute Uremia Dog with Complications

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Abstract: An 8 year-old, 20 kg, mixed breed dog presented with anemic condition, respiratory distress condition and severe uremia (BUN = 250 mg/dL, creatinine = 18.4 mg/dL) including anuria for 3 days. Hemodialysis treatments were performed 3 times at Hemodialysis unit, Kasetsart University Veterinary Teaching Hospital (KUVTH). The dialysis machine setting values including blood flow rate was set at 5 ml/kg/min, 5 ml/kg/min and 6 ml/kg/min, respectively. The dialysate flow rate was set at 500 ml/min in every session. The time was set at 90 minutes, 90 minutes and 150 minutes in each session, respectively. The urea reduction ratios were 0.48, 0.45 and 0.52, respectively. At the end of the treatment, the patient's azotemia level was on stage III of chronic renal disease (BUN = 37 mg/dL, creatinine = 3.17 mg/dL) with normal clinical signs. The time of hospital stay was 14 days. The patient could spend her life almost normally at home and lived 120 days. This case report had described details in the procedure of hemodialysis.

Keywords: Renal failure, Acute uremia, Hemodialysis

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Introduction

Hemodialysis is an advanced extracorporeal renal replacement therapy for uremic patients. This procedure can remove uremic toxins, correct fluid and electrolyte imbalance, and restore acid-base balance (Elliott, 2000). Importantly, hemodialysis can extend the life of uremic patients so that veterinarian has time to resolve the cause of acute uremia as well as renal functions begin to recover. Recovery of adequate renal function usually occurs within 2-4 weeks from the starting of dialysis (Sykes *et al.*, 2011). However, hemodialysis is costly and difficult to predict the outcome. The patients usually are applied with hemodialysis at the late

stage of disease, when medical management has failed. Renal replacement therapy is indicated in dogs with inadequate urine output that are developing volume overload, hyperkalemia, blood urea nitrogen (BUN) >80 mg/dL, or signs of uremia that are not responsive to medical management (Sykes *et al.*, 2011). Although usefulness of hemodialysis is obvious, technique of the procedure are crucial.

The hemodialysis system is based on three components: blood, membrane and dialysate (Ronco and Clark, 2001). Blood flow rate, dialysate flow rate and dialyzer efficiency including time of dialysis in each session are factors which effect the urea clearance. All these factor values are set by the physician who understands complications and all details about their patients. However, rapid removal of urea during hemodialysis results in rapidly reduction in serum osmolality. This can induce water to move into the cells and subsequent cerebral edema (Tuchman *et al.*, 2013). Therefore, the process of machine set up is crucial for hemodialysis efficiency.

The aims of this study was to provide technical information especially how to select the central venous catheter and outcome of intermittent hemodialysis in our practice nowadays.

Materials and Methods

Case history

An 8 year-old, 20 kg, intact, female mixed breed dog was referred to Kasetsart Veterinary Teaching Hospital (KUVTH) for progressive azotemia and acute anuria. Two weeks previously, the dog had been examined by a referring veterinarian because of vomiting and diarrhea. She was an indoor dog with no prior medical history. There was no other toxin exposure and dog was up-to-date on vaccinations. On initial presentation, results of the physical examination were depression, edema at ventral area of the body, mild dyspnea, anuria, body condition score 3.5/5, pink mucous membrane, dehydration <5 %, subnormal temperature (97°F), normal heart sound, heart rate 140 beats/min, moist lung sound and 94% SpO_2. The complete blood count and serum biochemistry were revealed in Table 1 and Table 2, respectively. The urine by cystocentesis revealed specific gravity at that time 1.015, protein +3, red blood cells >20 cells/hpf, white blood cells >20 cells/hpf and bacteria +3. The parvovirus test kit was also performed and shown a negative result. Abdominal ultrasound examination revealed thickening and brightening in both renal cortices. The acute renal failure (ARF) was suspected. The diagnosis was based on a short duration of signs, the significant

Table 1 Results of complete blood count analyses from the dog with anuric acute renal failure during hospitalization and after discharged

Parameter	Reference interval	Days								
		1	3	5	6	8	12	14	21	46
Hematocrit	35-55 %	24.3	21	24.7	24.2	25.4	24.4	25	34	38.5
Plasma protein	6-7.5 gm%	8.6	6.6	6.6	7	7.4	7	7.6	7	7
WBC	6000-17000 $\times 10^3$ /cumm	6.79	9.43	8.2	6.73	10.8	13	NA	7.19	6.63
Platelets	200-500 $\times 10^3$/µl	420	302	267	261	256	299	NA	367	58.8

NA = not applicable

Table 2 Results of serum biochemistry analyses in a dog with anuric acute renal failure during hospitalization and after discharged

Blood chemistry	**Reference interval**	**Day 0**	**Day 3**		**Day 6**		**Day 8**		**Day 13**	**Day 20 (Follow-up)**	**Day 46 Thrombocytopenia before progressed azotemia**
			Before HD	After HD	Before HD	After HD	Before HD	After HD			
BUN	10-26 mg%	250	238	124	156	86	109	52	106	37	71
Creatinine	0.5-1.3 mg%	18.42	19.06	11.83	13.95	8.42	10.15	5.71	4.19	3.17	3.97
Phosphorus	2.5-5.0 mg%	NA	24.9	13.5	19.3	10.5	18.6	9.5	16.4	8.5	10.6
Albumin	2.3-3.2 gm%	2.8	2.1	2.8	2.3	2.5	2.4	2.8	3	2.9	2.4
APTT	10.8-18.4 second	NA	19.2	NA	18.4	NA	NA	NA	NA	NA	NA
PT	3.5-7.5 second	NA	5.8	NA	6.9	NA	NA	NA	NA	NA	NA
TT	11.3-28.1 second	NA	28.1	NA	21.1	NA	NA	NA	NA	NA	NA

NA = not applicable, BUN = blood urea nitrogen, HD = Hemodialysis, APTT/PT/TT from coagulation laboratory at KUVTH

azotemia and the inappropriate urine concentration. The patient subsequently was admitted to the hospital and referred to the urologic clinic, KUVTH that day. Upon admission, the patient was given intravenous fluid for correcting dehydration. The bacterial infection was controlled by using metronidazole (15 mg/kg IV, q12h) and enrofloxacin (10 mg/kg SC, q24h). The dog was induced diuresis by using furosemide (2 mg/kg IV, q8h). The urine output following diuresis induced by furosamide was 0.8 ml/kg/hr. The hemodialysis was planned to start due to fluid retention.

Evaluation and preparation of patient before hemodialysis session

The intermittent hemodialysis (HD) was planned due to the progressive azotemia and documented anuria on day 3, 6 and 8. All the vital signs and blood profile including PT (prothrombin time), APTT (activated partial thromboplastin time), TT (thrombin time), CBC (complete blood count), blood chemistry and body weight of the patient were completely examined before every session. First session, the patient had serious complications, including anemia (HCT=21%), respiratory distress due to pneumonitis or pulmonary edema (Figure 1) and prolonged APTT. These complications can lead to hypotension, hypoxemia and bleeding during the dialysis session. Therefore, in the first session the fresh whole blood and oxygen supplement were prepared to support the patient. Moreover, body weight of the patient was recorded and considered before and after in every session. The information of body weight was useful for estimating the water retention and also for setting the ultrafiltration volume which was important for removing water from the patient.

Central venous catheterization (CVCs)

The temporary intravenous double lumen catheter for hemodialysis was made from polyurethane (Joline®). The size of the catheter was selected based on the size of patient. The outer diameter of catheter was 11 Fr (3.67 mm.). The length of the catheter was selected based on the landmark. The landmark was defined as the distance between the half part of the neck and the third rib. This distance measurement was used to determine the length of the catheter. When the catheter was placed on the jugular vein at the half of the neck, the tip of catheter should be at the anterior of the heart of the patient. The 15 cm length catheter was selected for this case. After preparation of the catheter by flushing the heparinized saline into the lumen, anesthesia was induced with diazepam (0.5 mg/kg IV, bolus) and propofol (2 mg/kg IV, bolus). The patient was on right lateral position where the landmark was clearly visible and aseptic. The

method for direct insertion into the jugular veins was used by the modified Seldinger technique (Seldinger, 1953). The tip of catheter was showed in Figure 1. The patient underwent hemodialysis on her right jugular vein immediately after the dialysis prescription was completely set.

Hemodialysis procedure

The hemodialysis procedure included dialysis machine (Fresinius 4008B), pediatric blood line set (Kawasumi), and dialyser (Nipro hiflux 90E). In the first session of dialysis, hrthe fresh 100 cc. of fresh whole blood was used to prime the circuit. Moreover, patient was given heparin, the anticoagulant for preventing the clot in the circuit. The anticoagulant was started with loading dose of undiluted heparin 50 units/kg by injected into the bloodline 5 minutes before initiating the dialysis. The maintenance dose of heparin was calculated for a total of 1.5-hour dialysis at the dose of 50 unit/kg/hr (Cowgill and Francey, 2012) and diluted with normal saline (1:10) then injected into the circuit every 10 minutes. The blood flow rate was set at 3 ml/kg/min initially in the first 30 minutes for every session until the vital signs were stable. Then, the rate was increased to 5 ml/kg/min. Time of dialysis was set at 90 minutes in the first and second session and 150 minutes in the third session depended on the patient tolerance while receiving the dialysis. Therefore, vital sign monitoring is very important. Ultrafiltration volume in each session were set at 1.2L, 0.4L and 0.7L, respectively.

Results

There were no hypotension and other complications happened during each session. Moreover, the blood flow was very smooth during the first and second session. There was no sign of occlusion by the thrombi. However, there was mechanical disruption by thrombi at the beginning of the third session. The heparinized saline was used to release the occlusion of thrombus in the catheter until the lumen was clear enough to continue the dialysis. The urea reduction ratio were 0.44, 0.47 and 0.52 in each session, respectively (Table 3). The urine output was monitored every day as shown in Table 4. The patient was discharged from the hospital on day 14 with urine output 2.15 ml/kg/hr. Moreover, the dog began to be thrombocytopenia (platelets 58.8 $\times 10^3$/µl) at day 46 and died on day 120.

Discussion

In our study, this acute uremic renal failure dog was dialysed 3 times during 14 day-hospitalization. According to the end of the dialysis, the patient's azotemia level was on stage III of chronic renal disease (CKD) (IRIS,

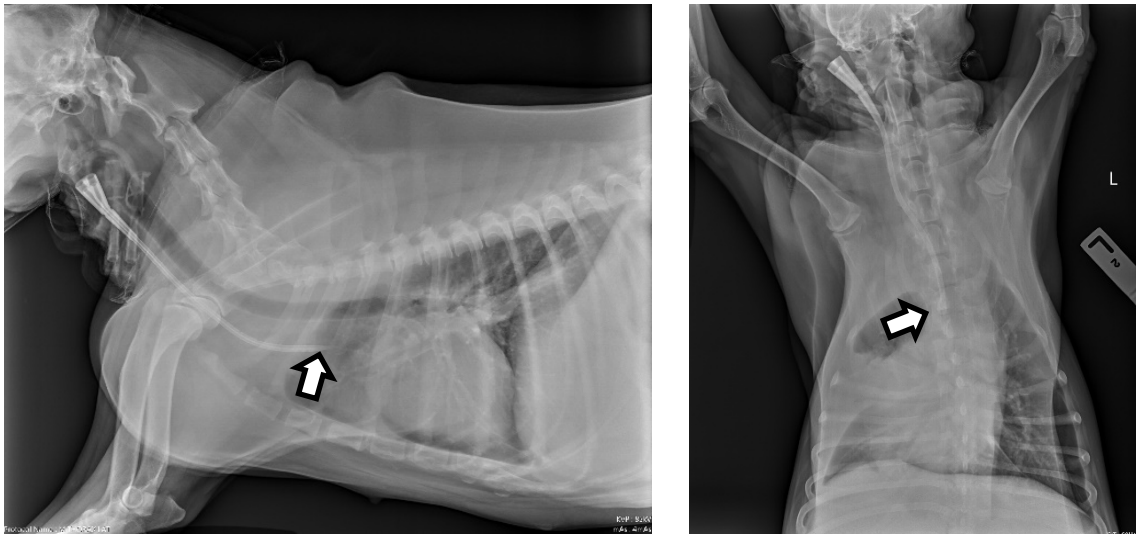

Figure1 Thoracic radiography showing abnormality opacity at right middle lung lobe on day 8 and showing position of the tip of jugular catheter.

Table 3 The records of hemodialysis components in each session

Dialysis No.	Time (minutes)	Qb (ml/kg/ minutes)	Qd (ml/minutes)	URR	Dialyser (surface area; m^2)
1	90	5	500	0.48	0.9
2	90	5	500	0.45	0.5
3	150	6	500	0.52	0.5

Qb = Blood flow rate, Qd = Dialysate flow rate, URR = Urea reduction ratio; (Pre-dialysis BUN-Post-dialysis BUN) / Pre-dialysis BUN

Table 4 The records of urine output during hospitalization.

Urine output	Days												
	1	2	3	4	5	6	7	8	9	10	11	12	13
ml/kg/hr	0	0.8	0.1	0.2	0.68	0.93	1.03	0.85	1.57	2.06	1.93	2.28	2.15

2016) with normal clinical signs. The patient could spend her life almost normally at home. The survival time after discharged from KUVTH was 120 days. The results from the previous study of 93 dogs and 42 cats with acute kidney injury treated with intermittent hemodialysis revealed the median duration of hospitalization were 9 days (range 1 to 45 days) in dogs and 8 days (range 1 to 23 days) in cats. The median number of treatments were 4 times (range 1 to 52 treatments) in dogs and 3 times (range 1 to 34 treatments)

in cats. The median survival time after hospital discharge was 9 days (95% CI=0 to 55 days) for dogs and 7 days (95% CI=0 to 835 days) for cats (Eatroff *et al.*, 2012).

The diagnosis of acute phase of chronic renal failure in this case was based on acute and rapid progression of the clinical signs including vomiting, diarrhea, anuria and severe azotemia. The diagnosis could not be concluded due to lack of previous medical history of the patient. However, the cause from bacterial infection could not be confirmed because urine culture was not performed on the first day.

The cause of death in this case was unknown. However, the patient had shown sign of normocytic normochromic anemia which might be resistant to erythropoietin administration, and progressed thrombocytopenia in 2 weeks before azotemia (Table 2). The presumptive cause of anemia and thrombocytopenia in this case might be Ehrlichiosis. The study of 19 dogs with chronic ehrlichiosis exhibited bicytopenia or pancytopenia, bone marrow hypoplasia, seroreactivity to Ehrlichia canis (E. canis) antigens, and no history of drug or radiation exposure, anorexia, depression, severe bleeding tendencies, hypoalbuminemia, and increased serum alanine aminotransferase activity were hallmarks of the disease (Mylonakis *et al.*, 2004). Nonetheless, no evidence of laboratory result was confirmed except non-regenerative anemia and thrombocytopenia. The bone marrow biopsy should be performed to rule out other causes of bone marrow disease.

For the complications of prolonged APTT, it might be caused by the condition of uremic crisis, pneumonitis or enteritis which might lead to DIC (Disseminated intravascular coagulation). However, only APTT test alone can has abnormalities due to unrelated disease or artifact (Donahue and Otto, 2005). In human, the study of 39 patients treated with hemodialysis without heparinization found that the treatment of patients 2 out of 3 were aborted before appropriate time due to the blood clot in the bloodlines and dialyser. Although, heparin is cleared with a half-life of 60 to 90 minutes in the bloodstream and can effect APTT as well as ACT (Activated coagulation time) (Cook, 2010). In this case, the lowest dose of heparin used in the circuit of hemodialysis was selected due to prolong APTT. The monitoring of blood loss including hematocrit, plasma protein and platelet count were repeated before and after each session. The clotting factor test was done 2 times and only before hemodialysis started due to the high cost of test. The study in human, described the monitoring of

coagulation parameters in hemodialysis patients might help in determining the risk of development of bleeding complications and increased morbidity rate (Khalid and Zafar, 2015). Therefore, clotting factor test might be used as a guide for management of the patient during and after the dialysis.

According to the component of hemodialysis such as blood flow rate, dialysate flow and ultrafiltration in each session was depended mainly on the clinical signs of the patient. In this case, there were three clinical considerations influencing the hemodialysis prescription. For anemia condition at the beginning, the dog was given stored whole blood 100 ml. to prime the circuit during the first hemodialysis. The advantages for priming the circuit with blood or other volume-expanding fluid are minimizing hypotension and hypovolemia (Cowgill and Francey, 2012). For respiratory distress condition, the dog was given the oxygen supplementation by a collar method before and during the session. Due to severe uremia (BUN 100-250 mg/dL), the dog was set shorter timing of dialysis in the first and second dialysis session and then fixed dialysate flow at 500 ml/min and set slow blood flow rate for minimizing the risk of dialysis disequilibrium. The previous study recommendation for an appropriate blood flow rate should be 1.5 to 2.0 ml/kg/min for initial treatment if the BUN concentration is between 150 and 300 mg/dL. The rate could be increased cautiously to 5 ml/kg/min in third and subsequent treatment (Cowgill, 2011). The dog was closely monitoring for the vital signs including body temperature, blood pressure, SpO_2, heart rate, mucous membrane color and neurologic complications. There were no abnormal complications during the dialysis session.

In conclusion, this case would provide the useful information for veterinarians and specialists to know the benefit of hemodialysis including how to prepare and prevent the complications. The application of hemodialysis can be applied for acute uremic crisis of chronic renal disease and other indications. The prognosis for recovery from renal failure in dogs depends on the etiology, extent of renal damage, co-morbid diseases, and presence of multiple organ system involvement. Moreover, the hemodialysis is an alternative or chance of increased survival for dogs nowadays in Thailand.

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