HEMODIALYSIS IN VETERINARY MEDICINE: REVIEW

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Abstract

Hemodialysis is used for the management of acute and chronic renal failure that is refractory to conventional medical therapy. For the moment, there are two types of hemodialysis: intermittent and continuous hemodialysis. Intermittent hemodialysis (IHD) is a renal replacement therapy that is defined by short and efficient hemodialysis sessions with the goal of removing endogenous or exogenous toxins from the bloodstream. IHD is indicated in cases of acute azotemia, electrolyte abnormalities or acidosis unresponsive to medical management. Continuous renal replacement therapy (CRRT) is a continuous process and, once treatment begins, therapy continues until renal function returns or the patient is transitioned to intermittent dialysis. The most common indication for CRRT is the treatment of acute kidney injury (AKI) in cases in which renal function is expected to return in the near future or for patients who are to be transitioned to IHD. Vascular access is the first and most basic requirement of successful extracorporeal renal replacement therapy (ERRT) and usually the jugular vein is used. Another vascular access consists of arteriovenous (AV) fistula or graft and it is the preferred access in patients with chronic hemodialysis. The ERRT catheter should be used only for ERRT procedures and handled only by ERRT personnel. When patients undergo IHD, their blood is removed from their bodies and run through an extracorporeal circuit. The blood is exposed to foreign material that may activate the clotting cascade. Therefore, anticoagulant therapy is often required during a dialysis treatment and special equipment is necessary for monitoring the level of anticoagulation. Complications of IHD have been widely reported and include hypotension and hypovolemia, vascular access problems and neurologic, respiratory, hematologic and gastrointestinal complications. The most significant complications of CRRT is coagulation. Despite appropriate heparin management, clotting of the CRRT circuit is inevitable.

Key words: hemodialysis, acute kidney injury, central venous catheter, anticoagulation, complications

INTRODUCTION

Dialysis is the process of separating a substance with colloidal dispersion from particles with molecular dispersion, based on the membrane properties to retain only the colloidal particles. This is used for artificial kidney function replacement. The kidneys role is to filter waste and toxins from the blood, concentrate or dilute urine, prevent dehydration or overhydration, regulate blood pressure and produce certain hormones.

Hemodialysis is a therapeutic procedure that uses the extracorporeal circulation of a patient's blood to ameliorate the azotemia, fluid overload. electrolyte and acid-base abnormalities characteristic of the uremic syndrome. Hemodialysis is used for the management of acute and chronic renal failure that is refractory to conventional medical therapy. Additional applications include acute intoxications (e.g. ethylene glycol poisoning) preoperative conditioning and of renal

transplant recipients. Hemodialysis is a technically demanding procedure that requires an extensive array of sophisticated delivery equipment and specifically trained and dedicated staff to perform, monitor and ensure the integrity and safety of the procedure in critically ill patients (Elliott, 2000).

DOG HEMODIALYSIS HISTORY

The first hemodialysis was performed experimentally on dogs in 1913 by Abel, Rowntree and Turner on experimental dogs with an "artificial kidney" composed of celloidin tubes, the predecessor of the modem hollow fiber dialyzer (Cowgill and Langston, 1996). Its use in dogs began in 1960 and continued by the early 1970's; these efforts were directed to therapeutic applications. By the early 80's vascular access technique used was the Quinton-Scribner modified method: arteriovenous shunts (AV), but in the past 30 years, the use of double lumen central venous catheters have revolutionized the technique of hemodialysis on dogs, mostly because of its anatomical features (Cowgill, 2013). John Jacob Abel directed arterial blood from animal patients, mixed it with an anticoagulant, passed it through a device that divided the blood into straw-like semipermeable membranes that were suspended in fluid and then directed the blood back to the patient and demonstrated that the subject's blood could be altered by changing the composition of the fluid. The first clinical program dedicated to providing hemodialysis services for dogs was established in 1990 at the University of California-Davis. Technological advances of today's systems have established efficacy, tolerance and safety in animals undergoing hemodialysis (Cowgill, 2013).

In Romania, the first hemodialysis performed successfully in dogs occurred in the Faculty of Veterinary Medicine's Clinic in February 2014.

HEMODIALYSIS TYPES

At the moment, there are two forms of hemodialysis: intermittent hemodialysis and continuous hemodialysis.

Intermittent hemodialysis (IHD) is a renal replacement therapy that is defined by short and efficient hemodialysis sessions with the goal of removing endogenous or exogenous toxins from the bloodstream. Common indications for IHD include drug or toxin ingestion, acute or acute-on-chronic kidney injury and chronic kidney disease (CKD).

Sessions can be performed once, as is common with toxin ingestion, or can be repeated daily or every other day for several days or longer, as is often done for acute kidney injury (AKI). Sessions can be conducted 2 or 3 times a week for the duration of the patient's life, as may be selected for CKD. Sessions are traditionally 1 to 6 hours in length, but can be longer, depending on the stability of the patient and efficiency of the session. IHD is designed as a more efficient modality than continuous renal replacement therapy (CRRT), meaning that IHD sessions remove small dialyzable molecules (blood urea nitrogen [BUN], creatinine, phosphorus, electrolytes, and certain drugs and toxins) from the bloodstream more rapidly than CRRT. Between treatments (the interdialysis period), these dialyzable molecules may again increase in the bloodstream (Bloom and Labato, 2011).

Continuous renal replacement therapy (CRRT) is a more recently developed blood purification modality. CRRT is a continuous process, and once treatment begins, therapy continues until renal function returns or the patient is transitioned to intermittent dialysis. CRRT is similar to IHD because patient blood is divided into thousands of straw like semipermeable membranes contained within a dialyzer; however, whereas IHD is primarily a diffusive therapy, CRRT uses diffusion, convection and, to a lesser extent, adhesion, CRRT has several significant advantages compared with IHD. The slow and gradual nature of the technique provides better control of electrolytes and acidbase balance (Bellomo et al., 1995). The operation continuous more closely approximates the functioning of a normal kidney (Clark et al., 1994). The goal of IHD is to make dramatic changes in a patient's uremic. acid-base and fluid status over short periods using diffusion; therefore, significant quantities of pure dialysate must be produced onsite. This technique requires a sizeable investment in the purchase and maintenance of specialized water treatment facilities (Langston, 2002).

PRINCIPLES OF HEMODIALYSIS

The main forces used during HD are diffusion, convection and adsorption. In HD, diffusion is the most prevalent force for exchange of solutes and fluids; convection and adsorption generally play a minor role. During diffusion, solutes move from areas of high to low concentration. In their moves, solutes leave the blood or dialysate fluid compartment in which they had been dissolved, cross the dialysis membrane and enter the opposite fluid compartment. Blood solutes such as BUN, creatinine, and electrolytes diffuse across the semipermeable dialvzer membrane into dialysate, which is discarded. Solutes in high concentration in dialysate, such as bicarbonate and selected electrolytes, may diffuse across the dialyzer membrane according to their concentration gradient into blood. Diffusion is best at removing molecules with low molecular weight from the blood, including BUN and creatinine, sodium, potassium, phosphorus and magnesium. Blood traveling in semipermeable membranes of the dialyzer is exposed to positive transmembrane pressure, which pushes fluid (ultrafiltrate) and dissolved solutes out of blood, across the dialyzer membrane and into the dialysate, which is discarded. Convection, a prevalent force in CRRT but not in IHD, is best in removing molecules with low and middle molecular weight from the blood. Middle molecules include many inflammatory mediators, as well as uremic toxins (Yeun and Depner, 2000).

INDICATIONS FOR IHD AND CRRT

IHD may be appropriate when medical management fails to achieve a positive outcome. Therefore, IHD is indicated in cases of significant or rising azotemia, electrolyte abnormalities or acidosis unresponsive to medical management. IHD is also indicated in cases of oliguria and anuria in the lack of response of appropriate medical management. IHD is commonly used in the management of humans with CKD (Yeun and Depner, 2000). IHD is an uncommon but available therapy for management of CKD in veterinary patients. Indications for IHD in patients with CKD include reduction of chronic progressive azotemia, hyperkalemia and fluid overload, as well as stabilization before renal transplantation. IHD may become part of a routine treatment of patients with systemic inflamematory response syndrome, sepsis or other severe inflammatory conditions via filtration and removal of inflammatory mediators, or fluid overload and congestive heart failure via ultrafiltration and removal of excess intravascular fluid volume as well as apheresis (Groman, 2010).

The most common indication for CRRT is the treatment of acute kidney injury (AKI) in cases in which renal function is expected to return in the near future or for patients who are to be transitioned to IHD. CRRT is used for patients with leptospirosis, tumor lysis syndrome, heatstroke, pre- and postsurgical support of ureteral obstructions, as well as aminogly-coside and melamine toxicities (Johnson and Simmons, 2006). Recent studies showed that hemodialysis can work wonders in propylene glycol intoxications on dogs, if ethanol 20% in

bolus in alternated with CRRT (Claus et al., 2011). CRRT has also been used to treat patients with diuretic-resistant congestive heart failure; however, this treatment has not yet been evaluated in companion animals (Clark and Ronco, 2004). Toxin ingestion is a common cause of acute renal failure (ARF) in dogs (Stanley and Langston, 2008). Raisins and grapes have been reported recently as an underlying etiology for ARF in dogs, although the underlying mechanism of nephrotoxicity remains unknown (Penny et al., 2003; Eubig et al., 2005).

BLOOD FLOW RATE AND LENGTH AND FREQUENCY OF HEMODIALYSIS SESSIONS

One way to calculate desired efficiency of the initial session based on severity of uremia is via the urea reduction ratio (URR) to determine the volume of blood that needs to be processed through the dialyzer to achieve a certain percent reduction in BUN level (Langston et al., 2010). URR and the corresponding blood flow rate (L/kg body weight) needed to achieve that particular URR have been determined for dogs and cats using empirical data from the Companion Animal Hemodialysis Unit at the Veterinary Medical Teaching Hospital at the University of California-Davis. In IHD, blood flow rate is the primary determinant of small molecule clearance, including BUN and potassium clearance. Therefore, one way to begin a dialysis prescription is to determine a desired URR, determine the volume of blood per kilogram body weight the machine must process to achieve that desired URR, and determine the desired length of the session, which is often 1.5 to 2 hours for the first session, 3 hours for the second session, and 4 hours (cats) to 5 hours (dogs) for the third or fourth sessions. (Langston, 2002). Using the patient's body weight, desired blood volume to be processed, and desired length of the session, vou can set vour blood flow rate in mL/kg/min accordingly. Blood flow rate is often set low at the start of the session and is slowly increased to the prescribed blood flow rate in the first 30 minutes of the session, to avoid hypotension or nausea (Elliott, 2000). Cowgill (2008) and Elliott (2008) recommend blood flow rates as low as 1 to 2 mL/kg/min for animals with predialvsis BUN level greater than 180 mg/dL.

For IHD of patients with CKD, sessions are performed 2 or preferably 3 times per week, with twice-weekly sessions appropriate only for those patients with sufficient residual renal function to avoid significant rebound solute accumulation between dialysis sessions.

Blood flow rate targets can be set at 15 to 25 mL/kg/min if thepatient's starting BUN level and vascular access can tolerate this high rate. Targets for length of session are 4 hours in cats and 5 hours in dogs, again, if well tolerated by the patient (Langston, 2002: Cowgill, 2008). Cowgill (2008) and Elliott (2008) recommend prolonged, slow treatment sessions of up to 8 hours for small patients with severe uremia (BUN level >250 mg/dL), using blood flow rates less than 2 mL/kg/min. For acute and chronic IHD, longer sessions may be both feasible and desirable, depending on treatment goals. Between dialysis sessions. solutes do reaccumulate. Therefore, bloodwork must always be taken at the start and end of the dialysis session and between dialysis sessions, so that appropriate dialysis prescriptions and interdialysis treatments are optimized for each individual patient.

VENOUS ACCESS AND CENTRAL VENOUS CATHETERS (CVC)

Vascular access is the first and most basic requirement of successful extracorporeal renal replacement therapy (ERRT). An adequately functioning dialysis catheter allows for smooth and efficient patient management. Various materials can be used to make a catheter that is minimally thrombogenic, flexible, and nonirritating to the vessel wall. (Chalhoub et al., 2011). To allow simultaneous removal and return of blood, a dialysis catheter has 2 lumens. Although catheters are placed in a central vein, the lumen that provides blood egress from the body is generally referred to as the arterial port or access port and the lumen that provides blood return to the body is termed the venous port or return port. The arterial lumen is usually shorter than the venous return lumen to avoid uptake of blood returning from the dialyzer (access recirculation), which would decrease the efficiency of treatment. In

some situations, 2 single-lumen catheters are placed in separate vessels or in the same vessel to provide blood egress and return. In lumens with a single opening (at the tip or a side port). partial occlusion from thrombosis or a fibrin sheath can decrease catheter function to the point of it being unable to provide adequate dialysis. The risk of complete occlusion is lessened by having multiple ports. If the ports are positioned circumferentially around the catheter, even if the vessel wall is drawn against the ports on one side of the catheter. blood flow can continue on the opposite side. If the side ports are small, blood preferentially flows through the tip, making the side ports superfluous. If the side ports are large, they weaken the catheter, and increase the amount of heparin that diffuses out of the catheter between dialysis treatments (Depner, 2001).

Temporary catheters should more precisely be called nontunneled, noncuffed catheters. Depending on the type, a temporary catheter may function for up to 4 weeks. In most cases, a temporary catheter is the appropriate choice unless there is suspicion of preexisting chronic kidney disease and the owners are interested in chronic dialysis (Chalhoub et al., 2011).

Permanent hemodialysis catheters have an external cuff which is usually made of Dacron. The catheter is placed with a portion in a subcutaneous pocket, which separates the site where the catheter exits the skin from the site where the catheter enters the vessel by several centimeters. Permanent catheters may have the ends of the lumens separated, so that the intravenous portion acts like 2 separate catheters placed in the same vein. By having separated tips, side ports can be placed circumferentially on each lumen, and the increased flexibility of the tips and their movement with each cardiac cycle may help decrease fibrin sheath formation (Depner, 2001).

Another vascular access consists of arteriovenous (AV) fistula or graft is the preferred access in patients receiving chronic hemodialysis. An artery is surgically anastomosed to a vein with a section of autologous vein or synthetic graft (typically PTFE). Within approximately one month, endothelial cells line the graft, and the endothelial cells of the autologous vein segment take on characteristics of arterial endothelium instead of venous. The graft/fistula is then accessed by percutaneous puncture of the arterial and venous segments with large - gauge needles at each dialysis treatment. Between treatments, no anticoagulant is needed because blood is continually flowing through the graft/fistula. A model of AV fistula has been developed for canine hemodialysis, and a brachial-cephalic access could be considered for dogs receiving chronic dialysis (Adin et al. 2002).

CATHETER FLOW CHARACTERISTICS

Because flow is proportional to catheter diameter and inversely proportional to catheter length, it is desirable to select the largest diameter catheter that can be placed. Minor changes in catheter diameter cause very large changes in flow, based on the Poiseuille equation:

$$Q_b = \frac{(KxPxD^4)}{(LxV)}$$

where Q_b is blood flow; K, a proportionality constant; P, the change in pressure; D, the luminal diameter; L, the catheter length and V, the blood viscosity. A 19% increase in catheter diameter doubles the blood flow; a 50% increase causes a fivefold increase in blood flow (Depner, 2001).

CATHETER CARE AND MANAGEMENT

The ERRT catheter should be used only for ERRT procedures and handled only by ERRT personnel. At each ERRT treatment, the exit site should be inspected and cleaned with antiseptic solution. When the ERRT catheter is accessed at the beginning and end of each treatment or at any other time, the catheter ports should receive an aseptic scrub for 3 to 5 minutes. When not in use, the catheter is bandaged in place and completely covered (Chalhoub et al., 2011).

CATHETER PERFORMANCE

Catheter function can decrease over time if thrombosis or stenosis occurs gradually, or performance can decline abruptly. A simple way of monitoring function at each dialysis treatment is to record the blood speed when the pressure in the arterial chamber (prepump) is - 200 mm Hg. A gradual decline in the blood speed at a standardized pressure predicts catheter malfunction. The arterial pressure should be maintained above -200 to -250 mm Hg, because at more negative values, the pump speed indicated on the machine is probably higher than the actual blood flow. Catheter design should focus on lowering flow resistance by increasing internal diameter rather than by shortening length (Depner, 2001).

EXTRACORPOREAL REMOVAL OF DRUGS AND TOXINS

The type of extracorporeal therapy used can greatly affect the extent of drug and toxin removal. The available modalities include intermittent hemodialysis and three types of replacement therapies continuous renal (CRRTs). Intermittent hemodialysis is primarily a diffusive process, whereas CRRT uses a combination of diffusion, convection, and adsorption. The continuous modalities include continuous venovenous hemofiltration (CVVH), a purely convective modality; continuous venovenous hemodialysis (CVVHD), a diffusive modality: and continuous venovenous hemodiafiltration (CVVHDF), which combines the aspects of both convection and diffusion (Bugge, 2001).

Systemic pH levels, body fluid composition, tissue perfusion, residual renal function, and contribution of non-renal routes of elimination can affect clearance (Bouman, 2008). Clearance describes the theoretical volume of blood fromwhich a solute is removed per unit time (Goodman and Goldfarb, 2006). A patient's native clearance depends on the ability of that solute to pass across the glomerular basement membrane; it may be affected by tubular secretion or reabsorption and is a function of the molecular weight, charge, and urine flow rate (Bayliss, 2010; Choi et al., 2009).

ANTICOAGULATION

The most common anticoagulant used in veterinary IHD is unfractionated heparin. Another method of anticoagulation is regional anticoagulation with citrate. Citrate is infused into the patient's blood as it enters the extracorporeal circuit, and chelates calcium in the blood rendering it incapable of clotting. To prevent the patient from becoming hypocalcemic, calcium is restored as an infusion. Citrate is not used as often in IHD as in continuous therapies, but it may be useful in certain patients. When using citrate regional anticoagulation, the level of anticoagulation is assessed by measuring the ionized calcium concentration in the extracorporeal circuit. Once in the body, citrate is converted into bicarbonate; therefore, a chemistry analyzer capable of measuring both ionized calcium and pH becomes essential (Poeppel et al., 2011).

During intermittent hemodialysis, the patient's blood is exposed to many substances, including the dialysis catheter, blood tubing, chambers and headers, and the large surface area of the dialyzer membrane. These surfaces exhibit variable degrees of thrombogenicity (Suranyi and Chow, 2010). In order to deliver a safe and effective dialysis treatment, an appropriate level of anticoagulation must be achieved to prevent thrombosis of the extracorporeal circuit without causing excessive bleeding in the patient. Careful monitoring of the extractorporeal circuit during dialysis may provide many indicators of potential clotting problems. The simplest method of evaluation is visual inspection. Very dark blood within the circuit, streaks within the dialyzer or the presence of fibrin on the walls of the arterial or venous chambers may indicate clotting and should be further evaluated by flushing the circuit with saline while temporarily occluding the arterial blood line. (Ross, 2011).

In veterinary medicine, anticoagulation in routine intermittent hemodialysis typically consists of the systemic administration of a standard dose of heparin (10-50 U/kg) as a bolus 5 minutes before starting the dialysis treatment. Adequate anticoagulation is then maintained with a continuous infusion of heparin (10-50 U/kg/h) into the arterial limb of the circuit. The heparin infusion or bolus administration may be discontinued up to 30 minutes before the end of the treatment or continued throughout the treatment, depending on the patient's bleeding risk and the degree of clotting in the extracorporeal circuit (Ross, 2011).

In some patients presented for hemodialysis, systemic anticoagulation may be contraindicated. Patients who have recently (<48 hours) undergone surgery, biopsy or some other invasive procedure or patients with gastrointestinal hemorrhage, possible cranial trauma, pulmonary contusions or any evidence of active bleeding should not receive systemic anticoagulation because of the risk of inducing or exacerbating bleeding.

EQUIPMENT

There are several basic types of dialvsis machines. In general, dialysis machines are designed to be used either for intermittent hemodialysis (IHD) or for continuous renal replacement therapy (CRRT). Regardless of the model or manufacturer, all modern IHD machines have certain common characteristics. First, they all contain a display screen, which may be a touch screen on newer models. This screen displays the current dialysis treatment mode, all options available in that mode, treatment parameters, alarm conditions and any necessary instructions. During the dialysis treatment, the screen also displays treatment status (ie, time left, amount of fluid removed, catheter pressures, and so forth). The electrolyte solution is a highly concentrated salt solution containing sodium, chloride, glucose and other components as desired (potassium, calcium, magnesium). The machine operator sets the desired sodium concentration of the dialysate (within the limits of the machine of between 130 and 155 mEq/L) based on patient parameters. The sodium concentration can be readily adjusted to avoid large or rapid changes in the patient's serum sodium concentration. thus avoiding dramatic fluid shifts. Bicarbonate is incorporated separately because bicarbonate and calcium from the electrolyte concentrate are incompatible in a concentrated form without inducing precipitation, thus allowing the bicarbonate concentration to be adjusted independently from sodium concentration. generally within the range of 25 to 40 mEq/L. (Poeppel et al., 2011).

A well-maintained water treatment system is essential to provide a safe hemodialysis treatment. The patient is exposed to roughly 20 gallons (76 L) of water in an average dialysis treatment, so even trace amounts of impurities can have detrimental effects (Ward, 2002; Van Stone, 2004; Ward, 2008). Newer dialysis machines are capable of producing "ultrapure" dialysate. The dialysate made from purified water is filtered through a special membrane before it is passed into the dialyzer. Water and electrolytes are able to pass through the membrane, but any bacterial contaminants are excluded. The ultrapure dialysate is then delivered to the dialyzer that contains the patient's blood (Bommer and Jaber, 2006).

Because CRRT is intended to be provided over a longer treatment period (ie, 24 hours a day compared with 4-5 hours a day for IHD), a slower blood flow rate is generally selected. In addition, clearance with CRRT is influenced more by effluent rate than by blood flow rate, making a rapid blood flow rate unnecessary in most cases. Because the CRRT machines do not prepare dialysate, there is no need for internal conductivity meters. At the end of treatment, all of the fluid bags and blood lines are discarded, so there is no need for disinfecting or cleaning cycles for CRRT machines. One additional piece of equipment that should not be overlooked is a heat source. Patients undergoing IHD tend to be hypothermic due to their azotemia and hypotension. The temperature of the dialysate can be adjusted so that the patient's blood can be warmed (or cooled) as it passes through the dialyzer. Circulating water heating pads provide some (Poeppel et al., 2011).

COMPLICATIONS

Complications of IHD have been widely reported. and include hypotension and hypovolemia; problems with vascular access; and neurologic, respiratory, hematologic, and gastrointestinal complications (Cowgill and Elliott, 2000; Elliott, 2000). Hypotension and hypovolemia occur during IHD sessions as a result of ultrafiltration and large extracorporeal blood volumes and can persist during or between sessions as a result of blood loss (from bleeding secondary to uremic ulceration. overheparinization, coagulopathy or blood loss secondary to filter or line clotting in which not all extracorporeal blood volume can be returned to the patient). Approximately 50% of IHD cases have problems with hypotension and hypovolemia (Langston et al., 1997; Langston

2000). Respiratory signs can occur in IHD patients as a result of underlying disease, complications or IHD or both. Respiratory complications include uremic pneumonitis and pulmonary hemorrhage, pleural effusion and pulmonary edema, hypoxemia, hypoventilation, and pulmonary thromboembolism (PTE) (Elliott, 2000). Hypoxemia and hypoventilation can be caused by ventilatory failure in the critically ill or neurologically impaired patient; whereas hypoxemia can be caused by diffusion failure as a result of pulmonary hemorrhage, pneumonitis, infectious pneumonia, or edema, or ventilation-perfusion mismatch caused by PTE (West, 2008). Hematologic complications thrombocytopenia, including anemia, and leucopenia are also common in patients with IHD. Again, these complications can be caused by primary disease; anemia is a common sequel of CKD. Anemia and thrombocytopenia result from coagulopathy and vasculitis common with systemic inflammatory response syndrome and leucopenia can result from infectious or inflammatory processes. Thrombocytopenia can occur secondary to contact activation with the dialysis membrane, and promotion of the coagulation cascade as a result of diseasespecific or iatrogenic coagulopathy, whereas leucopenia can occur transiently as a result of white blood cell interaction with the dialysis membrane (Elliott, 2000). Gastrointestinal complications such as nausea, vomiting and inappetance are common in uremic animals and can also be a complication of dialysis-induced hypotension, DDS, dialysate contaminants and incompatible blood transfusion reactions (Elliott, 2000; Fischer et al., 2004; Ross, 2010). The most significant complications of CRRT involve coagulation. Despite appropriate heparin management, clotting of the CRRT circuit is inevitable. Hypotension is another potential complication. Although the cause of the blood pressure drop at the start of therapy is likely to be multifactorial, the amount of blood needed to fill the CRRT circuit is at least partly the reason (Sulowicz and Radziszewski, 2006). Regarding the catheter complications, clothing is one of the most common complications. Despite using the least thrombogenic materials possible, hemodialysis catheters have a high rate of thrombosis. Both ports of the catheter should be flushed with saline or heparinised saline after every use (approximately 10–12 mL for a large catheter, 3 to 6 mL for smaller catheters) to prevent intraluminal thrombosis (Beathard, 2001). Infections are the most dangerous catheter complication in hemodialysis patients and they are most probably the predominant cause of morbidity (Himmelfarb, et al., 2005). Instillation of antimicrobial solutions, such as citrate or heparin combined with an antibiotic, may reduce the risk of bacteremia (Donlan, 2001).

CONCLUSIONS

IHD is a useful and feasible modality to improve outcome in dogs and cats with kidney injury that do not respond adequately to medical management. The decision to pursue hemodialysis in patients with acute or acuteon-chronic kidney injury should be made as quickly as possible to improve the likelihood of a successful outcome. IHD requires thorough understanding of renal physiology, as well as the principles and machinery involved in dialysis.

CRRT is a relatively new extracorporeal blood purification modality for the treatment of AKI, fluid overload and toxin exposure. Although CRRT has both therapeutic and operational advantages compared with IHD, its intensive nature and the need for specialized 24-hour care will likely limit the availability of this modality to a small number of referral institutions.

Monitoring catheter performance should be a routine part of dialysis patient care. Duallumen catheters are the most commonly used method of vascular access for extracorporeal renal replacement therapy. They are fairly quick to place but require meticulous care for optimal function. The most common complications are thrombosis and infection.

Several methods to prevent extracorporeal circuit clotting during hemodialysis have been used, but unfractionated heparin remains the mainstay of anticoagulant therapy in both human and veterinary intermittent hemodialysis.

There are several different machines available for the performance of renal replacement therapy in veterinary medicine. Extracorporeal renal replacement therapies (IHD and CRRT) involve dedicated personnel who are familiar with the operations and maintenance of the equipment.

REFERENCES

- Abel J., Rowntree L., Turner B., (1914), On the removal of diffusible substances from the circulating blood of living animals by dialysis. J Pharmacol Exp Ther 1914;5:275–316.
- Acierno M.J., (2011), Continuous renal replacement therapy in dogs and cats. Veterinary Clinics of North America: Small Animal Practice, 41(1), 135-146.
- Adin C.A., Cowgill L.D., Treatment and outcome of dogs with leptospirosis: 36 cases (1990–1998), J Am Vet Med Assoc 2000;216(3):371–5.
- Adin C.A., Gregory C.R., Adin D.B., Cowgill L.D., Kyles A.E., (2002), Evaluation of three peripheral arteriovenous fistulas for hemodialysis access in dogs. *Veterinary Surgery*, 31(5), 405-411.
- Ash S.R., (2007), Fluid mechanics and clinical sussess of central venous catheters for dialysis - answers to simple but persisting problems. Semin Dial 2007; 20:237.
- Bayliss G., (2010), Dialysis in the poisoned patient. Hemodial Int 2010;14:158–67.
- Beathard G., (2001), Catheter thrombosis. Semin Dial 2001;14:441.
- Beathard G., (2001), The use and complications of catheters for hemodialysis vascular access: introduction. Semin Dial 2001;14:410.
- Beckel N.F., O'Toole T.E., Rozanski E.A., et al., (2005), Peritoneal dialysis in the management of acute renal failure in 5 dogs with leptospirosis. J Vet Emerg Crit Care 2005; 15(3):201–5.
- Behrend E.N., Grauer G.F., Mani I., et al., (1996), Hospital-acquired acute renal failure in dogs: 29 cases (1983–1993). J Am Vet Med Assoc 1996; 208(4):537–41.
- Bellomo R, Ronco C., (2002), An introduction to continuous renal replacement therapy. In: Bellomo R., Baldwin I., Ronco C., et al, editors, Atlas of hemofiltration. London: W.B. Saunders; 2002. p. 1–9.
- Bellomo R., Farmer M., Parkin G., Wright C., Boyce N., (1995), Severe acute renal failure: A comparison of acute continuous hemodiafiltration and conventional dialytic therapy. *Nephron*, 71(1), 59-64.
- Bellomo R., Ronco C., (2002), Nomenclature for continuous renal replacement therapy. In: Bellomo R, Baldwin I, Ronco C, et al, editors. Atlas of hemofiltration. London: WB Saunders; 2002. p. 11–4.
- Berg R.I.M., Francey T., Segev G., (2007), Resolution of acute kidney injury in a cat after lily (Lilium lancifolium) intoxication. J Vet Intern Med 2007;21:857–9.
- Blaufox M.D., Hampers C.L., Merrill J.P., (1966), Rebound anticoagulation occurring after regional heparinization for hemodialysis. Trans Am Soc Artif Intern Organs 1966;12:207–9.
- Bloom C.A., Labato M.A., (2011), Intermittent hemodialysis for small animals. *Veterinary Clinics of*

North America: Small Animal Practice, 41(1), 115-133.

- Bociu N.A., Bălăşcău B., Ivaşcu C., Micşa C., Viţălaru B.A., (2015), Comparison between anticoagulation protocols in dogs undergoing hemodialysis. *Journal* of *Biotechnology*, (208), S43.
- Bogdan B.S., Bociu A., Ivaşcu C., Micşa C., Viţălar, B. A., (2015), Heparinization of the central venous catheter in dogs undergoing hemodialysis. *Journal of Biotechnology*, (208), S42.
- Bogdan B.S., Corneliu T., Raluca Munteanu., Laurentiu C.A., Constantin P.S., Nicolae, B.A., Vitalaru B.A., (2016), Choosing the dialyzer size in dogs undergoing hemodialysis. *Journal of Biotechnology*, (231), S80.
- Bommer, J., & Jaber, B. L. (2006, March), UNRESOLVED ISSUES IN DIALYSIS: Ultrapure Dialysate: Facts and Myths. In Seminars in dialysis(Vol. 19, No. 2, pp. 115-119). Blackwell Publishing Inc.
- Bouman C.S., (2008), Antimicrobial dosing strategies in critically ill patients with acute kidney injury and high-dose continuous veno-venous hemofiltration, Curr Opin Crit Care 2008;14:654–9.
- Brunet P., Simon N., Opris A., et al., (2008), Pharmacodynamics of unfractionated heparin during and after a hemodialysis session. Am J Kidney Dis 2008;51(5):789–95
- Brunet S., Leblanc M., Geadah D., et al., (1999), Diffusive and convective solute clearances during continuous renal replacement therapy at various dialysate and ultrafiltrate flow rates. Am J Kidney Dis 1999;34:486–92.
- Bugge J.F., (2001), Pharmacokinetics and drug dosing adjustments during continuous venovenous hemofiltration or hemodiafiltration in critically ill patients, Acta Anaesthesiol Scand 2001;45:929–34.
- Campbell A., Bates N., (2003), Raisin poisoning in dogs. The Veterinary record, 152(12), 376-376.
- Carson R.C., Kiaii M., MacRae J.M., (2005), Urea clearance in dysfunctional catheters is improved by reversing the line position despite increased access recirculation. Am J Kidney Dis 2005;45:883.
- Cerda J., Ronco C., (2009), Modalities of continuous renal replacement therapy: technical and clinical considerations. Semin Dial 2009;22:114–22.
- Chalhoub S., Langston C.E., Poeppel K., (2011), Vascular access for extracorporeal renal replacement therapy in veterinary patients. *Veterinary Clinics of North America: Small Animal Practice*, 41(1), 147-161.
- Choi G., Gomersall C.D., Tian Q, et al., (2009), Principles of antibacterial dosing in continuous
- Churchwell M.D., Mueller B.A., (2009), Drug dosing during continuous renal replacement therapy. Semin Dial 2009;22(2):185–8.
- Clark W.R., Mueller B.A., Alaka K.J., Macias W.L., (1994), A comparison of metabolic control by continuous and intermittent therapies in acute renal failure. *Journal of The American Society of Nephrology*, 4(7), 1413-1420.

- Clark W.R., Ronco C., (2004), Continuous renal replacement techniques. Contrib Nephrol 2004;144:264–77.
- Claus M.A., Jandrey K.E., Poppeng, R.H., (2011), Propylene glycol intoxication in a dog. *Journal of Veterinary Emergency and Critical Care*,21(6), 679-683.
- Congdon J.E., Kardinal C.G., Wallin J.D., (1973), Monitoring heparin therapy in hemodialysis. JAMA 1973;226:1529.
- Costea Ruxandra, Vitalaru B.A., (2015), Propofol induction anesthesia for central venous catheterization in dogs with renal failure. *Journal of Biotechnology*, (208), S42-S43.
- Cowgill L.D, Elliott D.A., (2000), Hemodialysis. In: DiBartola SP, editor. Fluid therapy in small animal practice. 2nd edition. Philadelphia: WB Saunders; 2000. p. 528–47.
- Cowgill L.D., (2008), Management of the chronic hemodialysis patient. In: Proceedings of the Advanced Renal Therapies Symposium. 2008. p. 1– 18.
- Cowgill L.D., Francey T., (2005), Acute uremia. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine. 6th ed. St. Louis: Elsevier Saunders, 2005:1731–1756.
- Cowgill L.D., Guillaumin J., (2013), Extracorporeal renal replacement therapy and blood purification in critical care. *Journal of Veterinary Emergency and Critical Care*, 23(2), 194-204.
- Cowgill L.D., Langston C.E., (1996), Role of hemodialysis in the management of dogs and cats with renal failure. *Veterinary Clinics of North America: Small Animal Practice*, 26(6), 1347-1378.
- Daugirdas J.T., Van Stone J.C., (2001), Physiologic principles and urea kinetic modeling. In: Daugirdas JT, Blake PG, Ing TS, editors. Handbook of dialysis. 3rd edition. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 15–45.
- Davenport A., (2004), Anticoagulation for continuous renal replacement therapy. Contrib Nephrol 2004;144:228–38.
- Davenport A., (2004), Replacement and dialysate fluids for patients with acute renal failure treated by continuous veno-venous haemofiltration and/or haemodiafiltration. Contrib Nephrol 2004;144:317– 28.
- Davenport A., (2009), Review article: low molecular weight heparin as an alternative anticoagulant to unfractionated heparin for routine outpatient hemodialysis treatments. Nephrology 2009;14:455– 61.
- Depner T.A., (2001), Catheter performance. Semin Dial 2001;14:425.
- Diehl S., Seshadri R., (2008), Use of continuous renal replacement therapy for treatment of dogs and cats with acute or acute-on-chronic renal failure. J Vet Emerg Crit Care 2008;18:370–82.
- Donlan R.M., Biofilm formation: a clinically relevant microbiological process. Clin Infect Dis 2001;33:1387.
- Drukker W., (1989), Haemodialysis: A historical review. In Maher JF (ed): Replacement of Renal Function by

Dialysis: A Textbook of Dialysis, ed 3. Dordrecht, Kluwer Academic Publishers, 1989

- Elliott D.A., (2000), Hemodialysis. Clin Tech Small Anim Pract. 2000;15: 136–148.
- Eubig P.A., Brady M.S., Gwaltney-Brant S M., Khan S.A., Mazzaferro E.M., Morrow C.M., (2005), Acute renal failure in dogs after the ingestion of grapes or raisins: a retrospective evaluation of 43 dogs (1992-2002), *Journal of veterinary internal medicine*, 19(5), 663-674.
- Fischer J.R., Pantaleo V., Francey T., et al., (2004), Veterinary hemodialysis: advances in management and technology. Vet Clin North Am Small Anim Pract 2004;34(4): 935–67.
- Fischer K.G., (2007), Essentials of anticoagulation in hemodialysis. Hemodial Int 2007;11: 178–89.
- Golper T.A., Marx M.A., (1998), Drug dosing adjustment during continuous renal replacement therapy. Kidney Int Suppl 1998;66:S165–8.
- Golpher T., (2002), Solute transport in CRRT. In: Bellomo R, Baldwin I, Ronco C, et al, editors. Atlas of hemofiltration. London: WB Saunders; 2002. p. 15–8.
- Goodman J.W., Goldfarb D.S., (2006), The role of continuous renal replacement therapy in the treatment of poisoning. Semin Dial 2006;19:402–7.
- Gorden L.A., Simon E.R., Rukes .JM., et al., (1956), Studies in regional heparinization. N Engl J Med 1956;255:1063.
- Groman R., (2010), Apheresis in veterinary medicine: therapy in search of a disease. In: Proceedings of the Advanced Renal Therapies Symposium. 2010. p. 26– 32.
- Grudzinski L., Quinan P., Kwok S., et al., (2007), Sodium citrate 4% locking solution for central venous dialysis catheters - an effective, more costefficient alternative to heparin. Nephrol Dial Transplant 2007;22:471.
- Hackbarth R.M., Eding D., Gianoli Smith C., et al., (2005), Zero balance ultrafiltration (Z-BUF) in blood-primed CRRT circuits achieves electrolyte and acid-base homeostasis prior to patient connection. Pediatr Nephrol 2005;20:1328–33.
- Hattersley P.G., (1966), Activated coagulation time. JAMA 1966;196:436–40.
- Hattersley P.G., Mitsuoka J.C., Ignoffo R.J., et al., (1983), Adjusting heparin infusion rates from the initial response to activated coagulation time. Drug Intell Clin Pharm 1983;17:632–4.
- Henderson L.W., (1979), Pre vs. post dilution hemofiltration. Clin Nephrol 1979;11:120–4.
- Himmelfarb J., Dember L.M., Dixon B.S., (2005), Vascular access. In: Pereira BJ, Sayegh MH, Blake P, editors. Chronic kidney disease, dialysis, transplantation. 2nd edition. Philadelphia: Elsevier Saunders; 2005. p. 341.
- Janssen M.J., Huijgens P.C., Bouman A.A., et al., (1993), Citrate versus heparin anticoagulation in chronic haemodialysis patients. Nephrol Dial Transplant 1993;8:1228.
- Johnson C., (2007), Dialysis of drugs. Verona (WI): Nephrology Pharmacy Associates; 2007.

- Johnson C., Simmons W., (2006), Dialysis of drugs. Ann Arbor (MI): Nephrology Pharmacy Associates; 2006.
- Johnson C.A., (2010), Dialysis of drugs. CKD Insights; 2010. p. 1-56.
- Kuang D., Ronco C., (2007), Adjustment of antimicrobial regimen in critically ill patients undergoing continuous renal replacement therapy. Yearbook of Intensive Care and Emergency Medicine 2007;2007(12):592–606.
- Langston C., (2002), Hemodialysis in dogs and cats, Compendium 2002;24:540–9.
- Langston C.A., Poeppel K., Mitelberg E., (2010), AMC dialysis handbook. New York: Animal Medical Center; 2010. p. 3.
- Langston C.E., (2002), Acute renal failure caused by lily ingestion in six cats. J Am Vet Med Assoc 2002;220(1):49–52.
- Langston C.E., Cowgill L.D., Spano J.A., (1997), Applications and outcomes of hemodialysis in cats: a review of 29 cases. J Vet Intern Med 1997;11(6):348–55.
- Li A.M., Gomersall C.D., Choi G., et al., (2009), A systematic review of antibiotic dosing regimens for septic patients receiving continuous renal replacement therapy: do current studies supply sufficient data? J Antimicrob Chemother 2009;64: 929–37.
- Liangos O., Gul A., Madias N.E., (2006), et al. Longterm management of the tunneled venous catheter. Semin Dial 2006;19:158.
- Lohr J.W., Schwab S.J., (1991), Minimizing hemorrhagic complications in dialysis patients. J Am Soc Nephrol 1991;2:961.
- Lok C.E., Thomas A., Vercaigne L., et al., (2006), A patient-focused approach to thrombolytic use in the management of catheter malfunction. Semin Dial 2006;19:381.
- Lopot F., Nejedly B., Sulkova S., et al., (2003), Comparison of different techniques of hemodialysis vascular access flow evaluation. Int J Artif Organs 2003;26:1056.
- Luchtman-Jones L., Broze J., (1995), The current status of coagulation. Ann Med 1995; 27(1):47–52.
- MacFarlane R.G., (1964), An enzyme cascade in the blood clotting mechanism, and its function as a biochemical amplifier. Nature 1964;202:498–9.
- Maher J.F., Lapierre L., Schreiner G.E., et al., (1963), Regional heparinization for hemodialysis. N Engl J Med 1963;268:451.
- Mehta R.L., (1994), Anticoagulation during continuous renal replacement therapy. ASAIO J 1994;40:931–5.
- Monaghan K.N., Acierno M.J., (2011), Extracorporeal removal of drugs and toxins. Veterinary Clinics of North America: Small Animal Practice, 41(1), 227-238.
- Oliver M.J., Mendelssohn D.C., Quinn R.R., et al., (2007), Catheter patency and function after catheter sheath disruption: a pilot study. Clin J Am Soc Nephrol 2007;2:1201.
- Parakininkas D., Greenbaum L.A., (2004), Comparison of solute clearance in three modes of continuous renal replacement therapy. Pediatr Crit Care Med 2004;5:269–74.

Penny D., Henderson S.M., Brown P.J., (2003), Raisin poisoning in a dog. Vet Rec 2003;152:308

- Pinnick R.V., Wiegmann T.B., Diederich D.A., (1983), Regional citrate anticoagulation for hemodialysis in the patient at high risk for bleeding. N Engl J Med 1983; 308(5):258–61.
- Poeppel K., Langston C.E., Chalhoub S., (2011), Equipment commonly used in veterinary renal replacement therapy. *Veterinary Clinics of North America: Small Animal Practice*, 41(1), 177-191.
- Reetze-Bonorden P., Bohler J., Keller E., (1993), Drug dosage in patients during continuous renal replacement therapy. Crit Care Med 2009;37(7):2268–82. renal replacement therapy: pharmacokinetic and therapeutic considerations. Clin Pharm 1993;24:162–79.
- Ricci Z., Ronco C., Bachetoni A., et al., (2006), Solute removal during continuous renal replacement therapy in critically ill patients: convection versus diffusion. Crit Care 2006;10:R67.
- Ricci Z., Salvatori G., Bonello M., et al., (2005), In vivo validation of the adequacy calculator for continuous renal replacement therapies. Crit Care 2005;9:R266– 73.
- Ronco C., Bellomo R., Homel P., et al., (2000) Effects of different doses in continuous venovenous haemofiltration on outcomes of acute renal failure: a prospective randomized trial. Lancet 2000;356:26– 30.
- Ronco C., Bellomo R., Ricci Z., (2001), Continuous renal replacement therapy in critically ill patients. Nephrol Dial Transplant 2001;16(Suppl 5):67–72.
- Ross S., (2010), Dialysis complications. In: Proceedings of the Advanced Renal Therapies Symposium. 2010. p. 53–4.
- Ross S., (2011), Anticoagulation in intermittent hemodialysis: pathways, protocols, and pitfalls. Veterinary Clinics of North America: Small Animal Practice, 41(1), 163-175.
- Sanders P.W., Taylor H., Curtis J.J., (1985), Hemodialysis without anticoagulation. Am J Kidney Dis 1985;5:32.
- Schetz M., Ferdinande P., Van den Berghe G., et al., (1995), Pharmacokinetics of continuous renal replacement therapy. Intensive Care Med 1995;21(7):612–20.
- Schrader J., Stibbe W., Armstrong V.W., et al., (1988), Comparison of low molecular weight heparin and standard heparin in hemodialysis/hemofiltration. Kidney Int 1988; 33:890.
- Schwab S.J., Onorato J.J., Sharar L.R., et al., (1987), Hemodialysis without anticoagulation. One-year prospective trial in hospitalized patients at risk for bleeding. Am J Med 1987;83:405.
- Seldinger S.I., (1953), Catheter replacement of the needle in percutaneous arteriography; a new technique. Acta Radiol 1953;39:368–76.
- Sherman R.A., Kapoian T., (2008), Dialysis access recirculation. In: Nissenson AR, Fine RN, editors. Handbook of dialysis therapy. 4th edition. Philadelphia: Saunders Elsevier; 2008. p. 102.
- Stanley S.W., Langston C.E., (2008), Hemodialysis in a dog with acute renal failure from currant

toxicity. *The Canadian Veterinary Journal*, 49(1), 63.

- Stokes J.E., Bartges J.W., (2006), Causes of acute renal failure. Compend Contin Educ Pract Vet 2006;28:387–96.
- Sulowicz W., Radziszewski A., (2006), Pathogenesis and treatment of dialysis hypotension. Kidney Int Suppl 2006;S36–9.
- Sungur M., Eryuksel E., Yavas S., et al., (2007), Exit of catheter lock solutions from double lumen acute haemodialysis catheters - an in vitro study. Nephrol Dial Transplant 2007;22:3533.
- Suranyi M., Chow J.S., (2010), Review: anticoagulation for haemodialysis., *Nephrology*, 15(4), 386-392.
- Tolwani A.J., Wille K.M., (2009), Anticoagulation for continuous renal replacement therapy. Semin Dial 2009;22:141–5.
- Vaden S.L., Levine J., Breitschwerdt E.B., (1997), A retrospective case-control of acute renal failure in 99 dogs. J Vet Intern Med. 1997;11:58–64.
- Van Stone J.C., (1994), Hemodialysis apparatus. In: Daugirdas JT, Ing TS, editors. Handbook of dialysis. Boston: Little, Brown and Company; 1994. p. 30–52.
- Von Brecht J.H., Flanigan M.J., Freeman R.M., et al., (1986), Regional anticoagulation-hemodialysis with hypertonic sodium tricitrate. Am J Kidney Dis 1986;8:196.
- Ward R.A., (2002), Water treatment for in-center hemodialysis including verification of water quality and disinfection. In: Nissenson AR, Fine RN, editors. Dialysis therapy. Philadelphia: Hanley & Belfus, Inc; 2002. p. 55–60.
- Ward R.A., (2008), Water treatment equipment for incenter hemodialysis: including verification of water quality and disinfection. In: Nissenson AR, Fine RN, editors. Handbook of dialysis therapy. 4th edition. Philadelphia: Saunders Elsevier; 2008. p. 143–56.
- Warkentin T.E., Levine M.N., Hirsh J., et al., (1995), Heparin induced thrombocytopenia in patients treated with low molecular weight heparin or unfractionated heparin. N Engl J Med 1995;332:1330–5.
- Wentling A.G., (2004), Hemodialysis catheters: materials, design and manufacturing. Contrib Nephrol 2004;142:112.
- West J.B., (2008), Respiratory physiology: the essentials. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 13–73.
- Willms L., Vercaigne L., (2008), Does warfarin safely prevent clotting of hemodialysis catheters? Semin Dial 2008;21:71.
- Yeun J., Depner T., (2000), Principles of dialysis, Dialysis and transplantation: a companion to Brenner & Rectors' the kidney, Philadelphia WB Sanders, 1-32.