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Dialysis: A life saving approach in renal failure

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Abstract
Peritoneal dialysis is a modality of renal replacement therapy that has been extensively used over the past years as a method of kidney replacement therapy for patients with end stage renal disease (ESRD). Dialysis works on the principles of the diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane. Blood flows by one side of a semi-permeable membrane and a dialysate or fluid flows by the opposite side. The counter-current flow of the blood and dialysate maximizes the concentration gradient of solutes between the blood and dialysate, which helps to remove more urea and creatinine from the blood. In this process, dialysate is instilled into the peritoneal cavity and through the process of diffusion and osmosis, water, toxins, electrolytes and other small molecules are allowed to equilibrate.

Keywords: ESRD, peritoneal dialysis, acute kidney injury, uremia, urea kinetic

Introduction
In Medicine, dialysis (from Greek "dialusis", meaning dissolution, "dia", meaning through, and "lusis", meaning loosening) is primarily used to provide an artificial replacement for lost kidney function (renal replacement therapy) due to renal failure. Dialysis may be used for very sick patients who have suddenly but temporarily, lost their kidney function (acute renal failure) or for quite stable patients who have permanently lost their kidney function. When healthy, the kidneys maintain the body's internal equilibrium of water and minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, and sulfate) and the kidneys remove daily metabolic load of fixed hydrogen ions from the blood. The kidneys also function as a part of the endocrine system producing erythropoietin and 1, 25-dihydroxycholecalciferol (Calcitriol). Dialysis is an imperfect treatment to replace kidney function because it does not correct the endocrine functions of the kidney. Dialysis treatments replace some of these functions through diffusion (waste removal) and ultrafiltration [1].

With the widespread availability of dialysis, the lives of hundreds of thousands of patients with end stage renal disease (ESRD) have been prolonged. The leading cause of ESRD is diabetes mellitus, accounting for more than 40% of newly diagnosed cases of ESRD [2].The second most common cause is hypertension, which is estimated to cause 30% of ESRD cases. Other causes of ESRD include glomerulonephritis, polycystic kidney disease and obstructive uropathy [3].

Acute Renal Failure (ARF) is the most common indication for dialystic intervention in dogs [4].Without dialysis, animals with severe renal failure die with complication of uremia before repair can be achieved. Dialysis extends the life expectancy of these animals, allowing potential recovery [5]. The limited numbers of regional facilities providing dialytic services make their availability problematic but not impossible. Once indicated, the initiation of dialysis cannot be delayed. Selection of patients is based on subjective criteria predicting the likelihood for return of adequate renal function. 3 to 4 weeks of supportive care has been a historical benchmark for distinguishing reversible from irreversible renal failure. However, these criteria are now inadequate and must be redefined for patient receiving dialytic care. With dialytic support, some animals with seemingly irreversible disease can recover sufficient renal function with 4 to 6 months of treatment.

Animals with severe oliguria or anuria in which an effective diuresis cannot be initiated or maintained with replacement fluids, osmotic or chemical diuretics and renal vasodilators should be transferred immediately to a referral center where dialysis can be performed. Further attempts with conservative therapies are nonproductive, cause deterioration of the animal's condition, delay the start of dialysis and predispose the animals to life threatening hypervolemia [6]. Dialysis is also uniquely suited for the management of acute poisoning when the toxin is dialyzable.

Toxins and their metabolites can be removed rapidly and completely from the body with dialysis. hemodialysis is particularly effective for ethylene glycol intoxication and superior to treatment with either alcohol or 4-methypyrazole, which merely delays its metabolism without facilitating its removal from the body. Timely and aggressive hemodialysis can eliminate ethylene glycol and its glycolic metabolites within hours, preventing development of renal injury. Dialysis is the most effective therapy for managing animals with iatrogenic over hydration, life threatening edema or therapies requiring delivery of large volumes of fluids in animals with limited excretory capacity.

Principle

Dialysis works on the principles of the diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane. Blood flows by one side of a semi-permeable membrane and a dialysate or fluid flows by the opposite side [7]. Smaller solutes and fluid pass through the membrane. The blood flows in one direction and the dialysate flows in the opposite. The counter-current flow of the blood and dialysate maximizes the concentration gradient of solutes between the blood and dialysate, which helps to remove more urea and creatinine from the blood. The concentrations of solutes (for example potassium, phosphorus, and urea) are undesirably high in the blood, but low or absent in the dialysis solution and constant replacement of the dialysate ensures that the concentration of undesired solutes is kept low on this side of the membrane. The dialysis solution has levels of minerals like potassium and calcium that are similar to their natural concentration in healthy blood. For another solute, bicarbonate, dialysis solution level is set at a slightly higher level than in normal blood, to encourage diffusion of bicarbonate into the blood, to act as a pH buffer to neutralize the metabolic acidosis that is often present in these patients. The levels of the components of dialysate are typically prescribed by a nephrologist according to the needs of the individual patient.

Treatment option for renal failure patients

Commonly accepted criteria for putting on dialysis include the presence of the uremic syndrome, the presence of hyperkalemia unresponsive to conservative measure, extra cellular expansion, acidosis refractory to medical therapy, bleeding diathesis and creatinine clearance of <10 cc/min per $1.73m^2$. There is emerging consensus that patients with renal failure should be started on dialysis early although vigorous protein restriction can maintain the blood urea nitrogen at an acceptable level in these patients, it may come at the price of significant malnutrition, which in turn correlates with mortality on dialysis. In addition to carefully evaluating patients for the onset of uremia, regular measurement of renal function is important.

The treatment options available for patients with renal failure depend on whether it is acute or chronic. In acute renal failure, treatment includes hemodialysis. In chronic renal failure the options include hemodialysis, peritoneal dialysis, either as continuous ambulatory peritoneal dialysis (CAPD) or continuous cyclic peritoneal dialysis (CCPD), or transplantation. Although there are geographic variations, hemodialysis remains the most common therapeutic modality for ESRD. The choice between hemodialysis and peritoneal dialysis involves the interplay of various factors that include the patient's age.

Hemodialysis

In Hemodialysis, the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semi-permeable membrane. The cleansed blood is then returned via the circuit back to the body. Ultrafiltration occurs by increasing the hydrostatic pressure across the dialyzer membrane. This usually is done by applying a negative pressure to the dialysate compartment of the dialyzer. This pressure gradient causes water and dissolved solutes to move from blood to dialysate, and allows the removal of several litres of excess fluid during a typical 3 to 5 hour treatment [8]. Studies have demonstrated the clinical benefits of dialyzing 5 to 7 times a week, for 6 to 8 hours. These frequent long treatments are often done at home; while sleeping but home dialysis is a flexible modality and schedules can be changed day to day, week to week. In general, studies have shown that both increased treatment length and frequency are clinically beneficial [9].

There are three essential components to dialysis: the dialyzer, the composition and delivery of the dialysate and the blood delivery system.

Dialyzer

The dialyzer consists of a plastic device (fig. 1) with facility to perfuse blood and dialysate compartments (fig. 2) at very high flow rates. There are currently two geometric configurations for dialyzer: hollow fiber and flat plate. The hollow fiber dialyzers are composed of bundles of capillary tubes through which blood circulates while dialysate travels on the outside of the fiber bundle. In contrast, the less frequently utilized flat plate dialyzers are composed of sandwiched sheets of membrane in a parallel plate configuration. The advantage of the hollow fiber construction is the lower priming volume (60 to 90 ml vs. 100 to 120 ml for flat plate) and easier reprocessing of the filter for reuses in future dialysis treatments.

Recent advances have led to the development of many different types of membrane material. Broadly, there are four categories of dialysis membrane; cellulose, substituted cellulose, cellulo-synthetic and synthetic. Over the past two decades, there has been a gradual switch from cellulose derived to synthetic membrane, because the latter are more biocompatible. Biocompatibility may be defined as the ability of the membrane to activate the complement cascade. Cellulosic membranes are bio-incompatible because of the presence of free hydroxyl groups on the membrane surface. In contrast, with the substituted cellulose membranes, (e.g. cellulose acetate) or the cellulo-synthetic membranes, the hydroxyl groups are chemically bonded to either acetate or tertiary amino groups, resulting in limited complement activation. Synthetic membranes, such as polysulfone, polymethyl methacrylate and polyacrylonitrile membranes are more biocompatible because of the absence of the hydroxyl groups. Polysulfone membranes are now used in over 60% of the dialysis treatment [10].

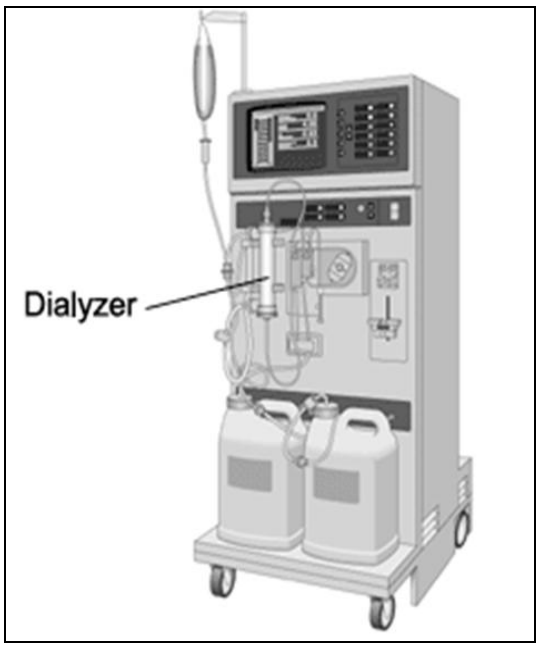

Fig 1: Dialyzer

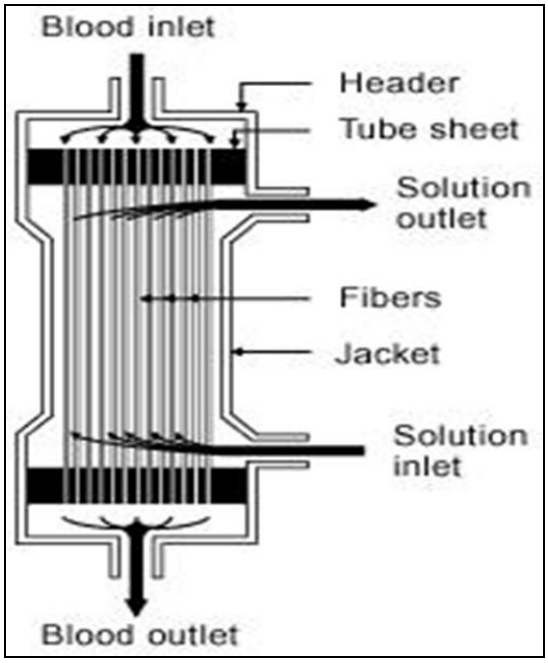

Fig 2: Campartments of a dialyzer.

Dialysate

The Composition of commercial dialysate for hemodialysate is given in Table 1. The potassium concentration of dialysate may be varied from 0 to 4 mmol/L depending on the predialysis plasma potassium concentration. The usual dialysate calcium concentration is 1.25 mmol/L. The usual sodium concentrations are associated with a higher frequency of hypotension, cramping nausea, vomiting, fatigue and dizziness. In patients who frequently develop hypotension during their dialysis run, sodium modeling to counterbalance urea related osmolar gradients is now widely used [11]. In this technique, the dialysate sodium concentration is gradually lowered from the range of 148 o 160 meq/L to isotonic levels (140 meq/L) near the end of the dialysis treatment. A dialysate glucose concentration of 200 mg/dL (11 mmol/L) is used to optimize blood glucose concentrations. Because patients are exposed to approximately 120 L of water during each dialysis treatment, untreated water could expose them to a dialysis centers, water used for the dialysate is subjected to filtration, softening, deionization and ultimately reverse osmosis. During the reverse osmosis process, water is forced through a semi permeable membrane at very high pressure to remove microbiologic contaminants and more than 90% of dissolved ions.

Table 1: Composition of commercial dialysate for hemodialysate

Solute	Bicarbonate Dialysate
Sodium (meq/L)	137-143
Potassium (meq/L)	0-4.0
Chloride(meq/L)	100-111
Calcium(meq/L)	0-3.5
Magnesium(meq/L)	0.75-1.5
Acetate(meq/L)	2.0-4.5
Bicarbonate(meq/L)	30-35
Glucose(mg/dL)	0-0.25

Blood delivery system

This is composed of the extracorporeal circuit in the dialysis machine and the dialysis access. The dialysis machine consists of a blood pump, dialysis solution delivery system and various safety monitors. The blood pump, using a roller mechanism, moves blood from the access site, through the dialyzer and back to the patients. The blood flow rate may range from 300 to 500 mL/min. Negative hydrostatic pressure on the dialysate side can be manipulated to achieve desirable fluid removal, so-called ultrafiltration [12]. Dialysis machine have different ultrafiltration coefficients (i.e. mL removed/min per mmHg) so that along with hydrostatic changes, fluid removal can be varied. The dialysis solution delivery system dilutes the dialysate concentration with water and monitors the temperature, conductivity and flow of dialysate.

Dialysis access

The fistula, graft or catheter through which blood is obtained for hemodialysis is often referred to as a dialysis access. A native fistula created by the anastomosis of an artery to a vein (e.g. the Cimino-Breschia fistula, in which the cephalic vein is anastomosis to the radial artery) results in arterialization of the vein. This facilitates its subsequent use in the placement of large needles (typically 15 gauge) to access the circulation. Although fistula have a high patency rate [13].

The dialysis access consists of an arteriovenous graft which interposes prosthetic material, such as polytetrafluoroethylene, between an artery and a vein. Such grafts have a 3 year patency rate of only 20%. Reasons for the higher rates of graft placement include the late referral of patients to vascular access surgeons so that by the time surgery is planned, the patient's arm veins have already been obliterated through multiple blood draws; the high prevalence of patients with diabetes mellitus and its associated microvascular disease; and the greater surgical skill required in creating a fistula. The most common access related complication is thrombosis due to intimal hyperplasia, which results in stenosis proximal to the venous anastomosis.

A double lumen cuffed catheter may be reasonable alternative to rather a native arteriovenous fistula or a graft in selected patients in which dialysis is required relatively urgently, such as patients who manifest delayed recovery from acute renal failure or where a further permanent access procedure is not feasible for anatomic reasons. Although double lumen catheters may permit blood flows comparable to a permanent arteriovenous access, these catheter are prone to infection and

to occlusion because of thrombosis. Temporary double lumen catheters in either the femoral vein or the internal jugular or subclavian vein are usually employed in patients with acute renal failure. The jugular is preferred to the subclavical vein because, for unclear reasons, a catheter placed in subclavical vein appears to be associated with a higher rate of venous stenosis. Temporary access can be for 2 to 3 weeks thrombosis, low blood flow and infection limit the life of the catheter.

Goals of dialysis

The hemodialysis procedure is targeted at removing both small and large molecular weight solutes. The procedure consists of pumping heparinized blood through the dialyzer at a flow rate of 300 to 500 ml/min, while dialysate flows in an opposite counter current direction at 500 to 800 ml/min. The clearance of urea ranges from 200 to 350 ml/min, while the clearance of β_2 microglobulin is more modest and ranges from 20 to 25 ml/min. The efficiency of dialysis is determined by blood and dialysate flow through the dialyzer, as well as dialyzer characteristics (i.e., its efficiency in removing solute) [14]. The dose of dialysis which is defined as the magnitude of urea clearance during a single dialysis treatment is further governed by patient size, residual renal function, dietary protein intake and the degree of anabolism and catabolism. Since the landmark studies of Sargent and Gatch relating the measurement of the dose of dialysis urea concentration with patient outcome, the delivered dose of dialysis has been corrected with morbidity and mortality. This has led to the development of two models for assessing the adequacy of the dialysis dose. Fundamentally, these two widely used measures of the adequacy of dialysis are calculated from the decrease in the blood urea nitrogen concentration during the dialysis treatment- that is, the urea reduction ratio (URR) and KT/V, an index based on the urea clearance rate, K and size of the urea pool, represented as the urea distribution volume, V. K, which is the sum of clearance by the dialyzer plus renal clearance, is multiplied by the time spent on dialysis. Currently, a URR of 65% and a KT/V of 1.2 per treatment are minimal standards for adequacy; lower levels of dialysis treatment are associated with increased morbidity and mortality [15].

For the majority of patients with chronic renal failure, between 9 and 12 hours of dialysis is required each week, usually divided into three equal sessions. However, the dialysis dose must be individualized. The measurement of dialysis adequacy KT/V or the URR serve only as a guide; body size, residual renal function, dietary intake, complicating illness, degree of anabolism or catabolism and the presence of large interdialytic fluid gains are important factors in consideration of the dialysis prescription.

Complications during hemodialysis

- Hypotension is the most common acute complication of hemodialysis.
- Muscle cramps during dialysis are also a common complication of the procedure.
- Anaphylactic reactions to the dialyzer, particularly on its first use, have been reported most frequently with the bioincompatible cellulose containing membranes.
- The major cause of death in patients with ESRD receiving chronic dialysis in cardiovascular disease. The rate of death from cardiac disease is higher in patients on hemodialysis as compared to patients on peritoneal dialysis and renal transplantation [3].

Peritoneal dialysis

Peritoneal dialysis (PD) is an alternative to hemodialysis for the treatment of end-stage renal disease [16]. In peritoneal dialysis, a sterile solution containing minerals and glucose is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a semi-permeable membrane [17, 18]. The dialysate is left there for a period of time to absorb waste products, and then it is drained out through the tube and discarded. This cycle or "exchange" is normally repeated 4-5 times during the day, (sometimes more often overnight with an automated system). Peritoneal dialysis is less efficient than hemodialysis, but because it is carried out for a longer period of time the net effect in terms of removal of waste products and of salt and water are similar to hemodialysis [19]. Its efficacy and possibility for at home performance make it the treatment of choice for many patients [20]. It does free patients from the routine of having to go to a dialysis clinic on a fixed schedule multiple times per week, and it can be done while traveling with a minimum of specialized equipment. Unfortunately, long-term therapy and repeated peritonitis episodes gradually cause morphology and functional changes of the peritoneum acting as a perm selective dialysis membrane [21].

Forms of peritoneal dialysis

Peritoneal dialysis may be carried out as continuous ambulatory peritoneal dialysis (CAPD), continuous cyclic peritoneal dialysis (CCPD) or nocturnal intermittent peritoneal dialysis (NIPD). In CAPD, dialysis solution is manually infused into the peritoneal cavity during the day and exchanged 3 to 4 times daily. A nighttime dwell is frequently instilled at bedtime and remains in the peritoneal cavity through the night. The drainage of spent dialysate is performed manually with the assistance of gravity to move fluid out of the abdomen. The major complication of CAPD is infectious peritonitis [22]. In CCPD, exchange are performed in an automated fashion, usually at night; the patients is connected to the automated cycler, which then performs 4 to 5 exchange cycles while the patients sleeps. Peritoneal dialysis cyclers automatically cycle dialysate in and out of the abdominal cavity. In the morning the patient, with the last exchange remaining in the abdomen is disconnected from the cycler and goes about his regular daily activities. In NIPD, the patients is given approximately 10 hours of cycling each night, with the abdomen let dry during the day.

Peritoneal dialysis solutions are available in various volumes ranging from 0.5 to 3.0 L. In peritoneal dialysis solution lactate is the preferred buffer. The most common additives to peritoneal dialysis solutions are heparin and antibiotics during an episode of acute peritonitis. Insulin may also be added in patients with diabetes mellitus.

Access to the peritoneal cavity

This is obtained through a peritoneal catheter. These are either acute catheters, used to perform acute continuous peritoneal dialysis, usually in an emergency setting or chronic catheter, which have either one or two Dacron cuffs and are tunneled under the skin into the peritoneal cavity. An acute catheter consists of a straight or slightly curved rigid tube with several holes at its distal end. Catheter can be inserted at the bedside by making a small incision in the in the abdominal wall; the catheter is inserted with the adhesive or suture. Complications occurring during dialysis, linked with catheter clogging with clots, fibrin and bends were the cause of dialysate retention in

the peritoneal cavity. Another complication occurring during dialysis therapy was subcutaneous leakage of the fluid close to the catheter, leading to local irritation and inflammatory states [23]. In contrast, chronic catheters are flexible and made of silicon rubber with numerous side holes at the distal end. These chronic catheters usually have two Dacron cuffs to promote fibroblast proliferation, granulation and invasion of the cuffs. The scarring that occurs around the cuffs anchors the catheter and seals it from bacteria tracking from the skin surface into the peritoneal cavity; it also prevents the external leakage of fluid from the peritoneal cavity [24]. The cuffs are placed in the preperitoneal plane and approximately 2 cm from the skin surface. The most common chronic peritoneal dialysis catheter in use is the Tenckhoff catheter, which contain two cuffs.

Conclusion

Hemodialysis is technically feasible, safe, efficacious and indispensable for the management of renal failure. The very nature of its complexity, costs and narrowly targeted applications will restrict widespread application of hemodialysis in veterinary practice. However, there is no alternative therapy as efficacious for animals with severe uremia, refractory oliguria, life threatening hypervolemia or acute poisoning. The increased awareness and acceptance of dialysis by veterinarians and animal owners is required for further expansion of use of hemodialysis in animal practice for the management of conditions associated with renal failure.

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