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Intermittent hemodialysis in a labrador retriever dog

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Abstract
Intermittent Hemodialysis (IHD) is a modality of renal replacement that has been used in the last decades among veterinarians in cases of drug or toxin ingestion, acute or acute-on-chronic kidney injury, and chronic kidney disease (CKD). The objective of the study was to evaluate the effect of intermittent hemodialysis instituted in a dog with CKD in order to provide a better quality of life. A nine years old Labrador retriever dog with chronic kidney disease at stage III received IHD treatments. Blood samples were collected before and after each session of IHD treatment. Intermittent hemodialysis remarkably decreased serum urea, creatinine, and phosphorus levels. Significant improvement was noticed in the patient with regards to clinical signs and symptoms, haemato-biochemical parameters and quality of life.

Keywords: intermittent hemodialysis, CKD, kidney, dog

Introduction
Hemodialysis works as an artificial kidney that ameliorate the azotemia, fluid overload, electrolyte and acid-base abnormalities by utilizing the extracorporeal circulation of a patient's blood. IHD has become a therapeutic alternative in the scenarios of failure of conventional clinical treatment, thus re-establishing the patient's homeostasis caused by uraemia and proving an improvement in quality of life (Langston, 2002) [19] and involves short, efficient hemodialysis sessions usually three times a week. Cowgill and Francey (2012) [9] has stated that dogs with chronic kidney disease submitted only to conservative treatment without the institution of IHD had rarely survived however, those undergoing IHD has shown longer survival period than expected for the disease.
IHD is designed as a more efficient modality comparing continuous renal replacement therapy (CRRT), by removing small dialyzable molecules including blood urea nitrogen, creatinine, phosphorus, electrolytes, and certain drugs and toxins from the bloodstream more rapidly than CRRT (Bloom and Labato, 2011) [2]. However, the catheter, equipment and procedure for IHD are expensive. The procedure also requires the trained personals. Some machine and accessory including the tubing line have limitation due to high extracorporeal volume and dialysis can be performed only in the medium to large breeds of dogs. IHD has been studied in veterinary medicine for over many years, showing scientific evidence that it can be a safe and effective technique (Cowgill & Guillaumin, 2013) [8]. The objective of this study was to evaluate the effect of intermittent hemodialysis in a dog with CKD stage III and to assess its outcome on quality of life.

Case report and observations
Nine years-old, male, 36.5 kg, Labrador retriever dog was referred to TVCC, Nagpur Veterinary College, Nagpur 440010. The dog's owner had a chief complaint of anorexia, vomiting and diarrhoea, dullness and lethargy, severe weight loss and anaemia past two weeks. The dog had a regular history of deworming, vaccination, no previous history of trauma or illness and was maintained on homemade+commercial diet. Clinical examination revealed moderated dehydration with rectal temperature of 101.5°F and SpO_2 - 93 per cent. Other physical parameters were within normal range. All mucous membranes were severely congested. Oral examination showed presence of ulcers and roupy salivation, dental tartar with halitosis. Dog was initially assessed for kidney function tests, electrolyte disturbance and changes in the haematological parameters. Further diagnostic work-up included abdominal ultrasonography and urinalysis was performed on the first day of treatment.
Based on the history, suspected aetiology, ultrasound findings, and urine specific gravity, the patient was diagnosed as of a case of chronic kidney disease. According to the IRIS staging of CKD, the present case was staged and treated as an IRIS CKD Stage III patient (IRIS Staging

of CKD (modified 2019)) having serum creatinine level of 4.0 mg/dl and UPC value of 2.55.

Table 1: Hemato-Biochemical parameters of the patient at the day of presentation**.**

Hemato-Biochemical Analysis	
Hemoglobin	09.90 gm%
TEC	3.94 x10^6/µl
PCV	26.10 %
TLC	14.9 x10^3/µl
Platelet Count	195 x10^3/µl
BUN	60.10 mg/dl
Creatinine	4.00 mg/dl
Phosphorus	11.7 mg/dl
Total calcium	9.90 mg/dl
Ionic Calcium	1.25 mmol/L
Sodium	133.00 mEq/L
Potassium	4.01 mEq/L
Chloride	107.00 mEq/L
Total Protein	4.10 gm/dl
Albumin	2.10 gm/dl
Globulin	6.00 gm/dl

Table 2: Urinalysis of the patient at the day of presentation

Complete Urinalysis	
Colour	Yellow
Glucose	Negative
Bile	Negative
Specific Gravity	1.010
Blood	Negative
Ph	6.0
Protein	3+
Nitrate	Negative
Uro	0.2Eu/dl
Leucocyte	Negative
Ketone	Negative
Pus Cells	08-09/hpf
Red blood cell	1-2/hpf
Urine Protein	112.80
Urine Creatinine	44.10
UPC	2.55

The patient was first subjected to conventional medical management in order to stabilise the initial clinical sign and symptoms. Dehydration was corrected according to the basic principle of fluid therapy (DiBartola, 2006) [12]. Vomiting was managed with proton pump blocker and antiemetic drugs. Human recombinant erythropoietin was prescribed to correct anaemia in combination with ferrous sulphate supplementation. Also, Tab Sevelamer Hydrochloride 50 mg/kg b.w. and Sucralfate 1 gm as mucosal protectant was given per orally twice a day till the serum phosphorus levels returned to normalcy along with a prescription kidney diet was prescribed to the patient.

Once the patient was stabilised, he was then subjected to hemodialysis and catheterised with a double-lumen catheter (size 12FR x 16 cm) in the left external jugular by employing Seldinger technique. The catheter was secured in place by suturing with surgical nylon (Chalhoub *et al.* 2011) [4]. The dialysis prescription was formulated on the basis of body weight, initial blood urea nitrogen and serum creatinine, PCV and platelet counts, etc. The intermittent hemodialysis was performed on a 4008S Fresenius Hemodialysis Machine, and the Hemoflow F6 HPS, Fresenius Medical Care hemodialyzer was used having a surface area of 1.30m^2 and priming volume of 78ml was prescribed. The blood tubing set used were designed for an adult human and manufactured by "Nipro Set™ Blood Tubing" had a priming volume of 158 ml. Thus the total extra-corporeal volume formed were 236 ml for F6 dialyzer. Total five sessions of intermittent hemodialysis was performed on the patient. The patient underwent sessions of IHD every alternate day. The dialysate flow rate was set constant at 500ml/min for all five sessions (Cowgill, 2011a) [6]. The clotting time was checked before initiating the dialysis. A heparin bolus of 40-50 IU/kg was prescribed for anticoagulation and maintenance was done @ 25-50 IU/kg/hr as a continuous rate infusion of heparinised saline (Ross, 2011) [24].

Blood samples were collected for hemato-biochemical analysis before each session of hemodialysis (PRE sample) and immediate and 30 minutes after the end of each hemodialysis session (POST sample). The dog was evaluated for urea reduction ratio (URR), Creatinine Reduction Ratio (CrRR), Kt/V and TAC_{urea} in order to estimate the efficacy of the chosen dialysis prescription. The dog was daily monitored for any clinical side-effect or complication due to the procedure and for any other clinical signs and symptoms.

Results and Discussion

Nine years-old, male, 36.5 kg, Labrador retriever dog was presented with the chief complaint of anorexia, frequent vomiting and diarrhoea, dullness and lethargy, severe weight loss and anaemia past two weeks. Kavitha *et al.* (2013) [18] identified various clinic-pathological changes in dogs with different stages of chronic renal disease and observed that anorexia, vomiting, melena, emaciation, pale mucosa, halitosis were the predominant signs in stage III and depression, emaciation, stomatitis, dehydration, vomiting, melena and nervous signs in stage IV of CKD. Oburai *et al.* (2015) [22] and Dunaevich *et al.* (2020) [14] also observed indistinguishable symptoms in dogs suffering from chronic renal failure viz. anorexia, followed by vomiting, dullness and weight loss, oral ulcer, hypertension, polyuria and polydipsia, recumbency and blindness.

On the basis of clinical signs and symptoms shown by the patient, initial hemato-biochemical analysis was performed to assess the extent of azotemia and electrolyte imbalance. The complete blood cell (CBC) count on day 0 revealed decreased levels of haemoglobin, Red Blood Cell (RBC) count, Packed Cell Volume, and Platelet count (Table 1). Total Leucocyte Count was within the normal referral range. These observations were in accordance with Stanley and Langston (2008) [25], Thakkar and Gaikwad (2014) [27], Melchert *et al.* (2017) [21] and Geraldes *et al.* (2019) [17] who also reported remarkably reduced value hemoglobin, hematocrit and packed cell volume in dogs chronic kidney disease who underwent hemodialysis. The authors reported a further decline in these values after hemodialysis sessions. Braun and Lefebvre (2008) [3] stated that the synthesis of EPO decreases in advanced chronic renal disease and is insufficient to meet the demands for new red cell production, resulting into anemia. Devipriya *et al.* (2018) [11] also noticed high significant reduction in packed cell volume, haemoglobin and erythrocyte count and increased values of total leucocyte count in dogs with renal insufficiency. The possible reason of these values could be attributed to the fact that non-regenerative anemia in dogs with chronic kidney disease and rehydration of patients through adjuvant fluid therapy leading to hemodilution could attribute to the decreased values of

PCV, TEC and hemoglobin. Deficiency of erythropoietin in CKD and deficient absorption of iron in the body is also one of the major causes of anemia in CKD.

The serum biochemistry showed marked increase in the Blood Urea Nitrogen (BUN) and Creatinine levels along with hypoproteinaemia, hyponatremia and hyperphosphatemia (Table 1). Devipriya *et al.* (2018) [11] also noticed high significant increase serum urea nitrogen, creatinine and phosphorus level and reduced values of total protein in the CKD affected dogs when compared with healthy dogs. According to Chew and Gieg (2006) [5] hyperphosphatemia is a frequent finding in patients with either acute renal failure or chronic renal failure and it can be as severe as 10mg/dl and it can be excessively severe when compared with the increase in BUN or serum creatinine concentration. An elevated level of serum phosphorus at 0^{th} day in the present study could be attributed primarily to an increased absorption of phosphorus in the intestines and decreased phosphate excretion through urine and secondary due to a transport of phosphate ions from the intracellular to extracellular compartment. Results of hyponatremia observed in the present study correlated with Martinez and Carvalho (2010) [20] and Sumit *et al.* (2018) [26] also observed significantly lower value of serum sodium in dogs with stage 3 and 4 of chronic kidney disease when compared to the other dogs. Chew and Gieg (2006) [5] opined that serum chloride concentration usually paralleled serum sodium concentration during free water loss. Pillai *et al.* (2012) [23] reported hypoproteinemia (3.40 gm%) and hypoalbuminemia (1.4 gm%) in a Labrador dog suffering from nephrotic syndrome. Hypoproteinemia is common in dogs with chronic kidney disease and the primary reason could be proteinuria which results due to malfunctioning of normal renal handling of proteins.

Urinalysis showed slight decrease in urine pH, isosthenuric specific gravity and presence of urinary protein, UPC ratio was 2.55 indicating proteinuria. Braun and Levebvre (2008) [3] opined isosthenuria as a frequent finding in dogs with chronic renal failure. According to Braun and Lefebvre (2015) the maximum limit of urinary protein in normal dog is around 6 mg/kg BW/day whereas DiBartola *et al.* (1980) [13] stated 14mg/kg/day of urinary loss of protein in a normal dog. The overall index of total urinary protein loss of an individual dog is estimated with the help of urine protein to creatinine (UPC) ratio. Grauer (2011) [16] opined normal protein excretion in dogs to be ≤ 10mg/kg/day with a normal UPC ratio of ≤ 0.2; however, a UPC ratio ranging between 0.2 - 0.5 in dog is considered as borderline proteinuria and those with UPC ratio > 0.5 is regarded as persistent proteinuria whereas UPC > 2.0 is a strong suggestion of glomerular disease.

On abdominal ultrasound, both the kidneys showed parenchymal changes with loss of cortico-medullary differentiation whereas rest other organs were normal in shape, size and echogenicity (Fig. 1). The size of the kidneys was also small and irregularly shaped. According to Finco *et al.* (1971) [15] both these observations i.e. smaller sized kidney with loss of corticomedullary junction indicates gradual loss of nephrons over a long period of time and are related with chronic nature of renal failure.

The intermittent hemodialysis prescription was formulated in order to minimize the degree of azotemia, normalize the fluid electrolytes imbalance and ameliorate the clinical signs in dog during each session. The details of intermittent hemodialysis prescription regarding the blood flow rate (Q_b), dialysate flow rate (Q_d) and length of dialysis session (T_d) for each session is tabulated in Table No.3. The dialysate flow rate (Q_d) by convention was kept constant at 500 ml/min as per suggested by Bloom and Labato (2011) [2] who mentioned that the Q_d can be altered if required in order to provide increased or decreased clearance. Intermittent hemodialysis was performed wherein the first session was kept less intensive with less solute removal, slower blood flow rate and shorter duration of time so as to allow the patient to get accustomed with the dialysis procedure and the change induced by the procedure (Langstan, 2002) [19]. The upcoming sessions were set for longer duration, with higher blood flow rate and were more intensive in terms of solute removal. Maximum five sessions were performed every alternate days i.e. three times a week until clinical recovery as recommended by Cowgill (2011a) [6].

Table 3: Hemodialysis Prescription for all Sessions and Pre and Post IHD of Blood Urea Nitrogen and Serum Creatinine Values

Session	Q_b (ml/kg/min)	Q_d (ml/min)	T_d (mins)	Blood Urea Nitrogen (mg/dl)		Serum Creatinine (mg/dl)	
				Pre IHD	Post IHD	Pre IHD	Post IHD
Session 1	1.78	500	120	60.1	42.03	4.0	2.9
Session 2	3.43	500	150	56.9	44.50	3.3	3.0
Session 3	4.29	500	180	52.1	48.00	3.8	2.9
Session 4	6.40	500	240	56.0	40.10	3.2	2.8
Session 5	5.42	500	180	47.3	26.81	3.0	1.5

The pre and post IHD values of (BUN) and serum creatinine of each session required for calculation of reduction ratio is depicted in Table No. 3. The details of the five sessions of intermittent dialysis with regards to the reduction ratio and the dialysis adequacy are documented in Table No.4.

Table 4: Immediate post and 30 mins Post IHD Reduction Ratio, Kt/V, spKt/V and eKt/V

Session	URR %		CrRR %		Kt/V	spKt/V	eKt/V
	Immediate Post IHD	30 mins Post IHD	Immediate Post IHD	30 mins Post IHD			
1	30.07	28.78	27.5	25	0.71	0.469	0.358
2	21.79	19.33	9.09	9.09	0.62	0.343	0.291
3	7.86	7.29	23.68	21.05	0.35	0.17	0.166
4	28.39	27.14	12.5	9.375	0.84	0.537	0.486
5	43.31	42.71	50	48.33	1.51	0.841	0.703

According to Langston (2002) [19], the aim of the first, second and additional sessions should be decreasing the BUN value by 25% to 33% in first session, 50% in second session and around 95% in additional sessions. According to Cowgill and

Francey (2006), a patient with initial BUN concentration <200 mg/dl must have a URR/hr of 12-15%/hr as a part of dialysis prescription. In contrast to this, the observed value of URR was higher in the first session than the recommended value and the URR/hr in the first session was also higher. The possible reason for higher URR could be longer duration of the session with slower blood flow rates. The URR was reduced in the second and additional sessions than the recommended value could be attributed to lower blood flow rate attained in the respective sessions. Other possible reasons could be the alterations in the blood flow rate to the dialyzer due to excessive movements of the dog causing kinking of the catheter and moving the tip of catheter out of the right atrium (Davenport, 2000) [10]. Fluctuations of blow flow rate in the arterial line caused reversal of the arterial and venous lines leading to recirculation that might have also affected the URR percent (Atapour *et al*. (2008) [1].

Although the difference between immediate and 30 minutes post IHD of BUN and serum creatinine of each session was minimal, the difference between 30 minutes post IHD BUN and creatinine of previous session and Predialysis BUN and creatinine of next session was observed to be much greater. This minor rebound noticed in each session could be an effect of performing high efficiency treatment in dog with low BUN concentration of at presentation for longer time period. According to Cowgill (2011b) [7], the benefits of IHD are short term, and the concentration of urea and all toxic solutes increases immediately with cessation of the dialysis session until new steady state is achieved or until the next dialysis session. The TAC BUN observed for the present dog was 49.52mg/dl having initial BUN value of 60.10 mg/dl with 4.13 L/kg of total blood processed in five sessions for total 14.50 hr/min. Thus, the adequacy of IHD was mildly effective in the dog. According to Cowgill (2011a) [6], a dog with a low predialysis BUN or TAC_{urea} represents high dialysis delivery (effective dialysis), improved renal functions with increasing residual renal clearance, low urea generation rate or protein catabolism rate or fluid overload.

The most common complications experienced was inadequate blood flow rate and recurrent fluctuations in the blood flow to the dialyzer as the dog was difficult to control and restrain without his owner nearby, and restricted movements of the dog for very long duration of session. Failure of the arterial line port causing catheter dysfunction wherein the aspiration of blood became difficult however, infusion was easy. As a result, the arterial and venous lines were exchanged leading to excess recirculation and again might have altered the reduction ratio. Kinking of catheter was seen during fourth session causing the tip of catheter to move out of the right atrium and hence the flow of blood was disturbed for the next cycle. Patient showed significant change in the biochemical parameters however, resolution of clinical signs such as regain of appetite and improved activeness were not so prominent, even during intra-dialytic sessions and the quality of life of the patient were insignificant. Owners could not afford the expensive treatment session as a part of future therapy and continued with the conventional treatment. However, the dog survived for 6 weeks after withdrawing the IHD treatment.

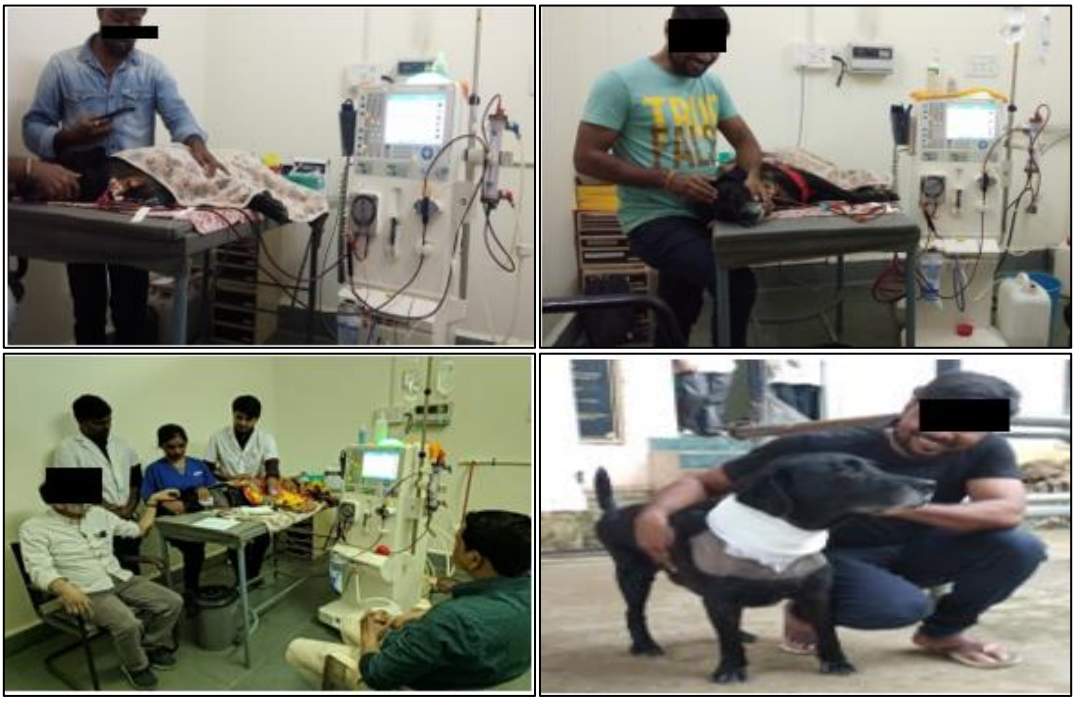

Fig 1: Blacky being dialysed and his post recovery image

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