The Pharma Innovation Journal 2022; SP-11(12): 28-30

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; SP-11(12): 28-30

www.thepharmajournal.com
Received: 08-10-2022
Accepted: 13-11-2022

M Ranjithkumar
Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

RC Sundararajan
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

K Gopal
Department of Veterinary Pathology, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

S Sunandhadevi
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

M Balgangatharathilagar
Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

M Kalaivanan
Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

E Madhesh
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

V Vijayanand
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

Advait Milind Swami
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

P Sainath
Department of Veterinary Medicine, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

Corresponding Author:
M Ranjithkumar
Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli, TANUVAS, Tamil Nadu, India

Therapeutic management of chronic kidney disease induced anemia using Darbepoeitin in a Labrador retriever

M Ranjithkumar, RC Sundararajan, K Gopal, S Sunandhadevi, M Balgangatharathilagar, M Kalaivanan, E Madhesh, V Vijayanand, Advait Milind Swami and P Sainath

Abstract
The present case study reports a therapeutic management of severe anemic crisis due to chronic kidney disease in a 4 years old male Labrador Retriever weighing 30 kg. The dog was presented with the history of decreased appetite, lethargy, depression and weight loss. Clinical examination revealed muscle wasting, pale conjunctiva, ozena and dehydration. Hemato-biochemical analysis showed severe anemia, hyperphosphatemia and renal azotemia. Ultrasound examination revealed shrunken kidneys with abnormal echogenicity and loss of corticomedullary junction. Based on the clinical findings, hemato-biochemical findings and abdominal ultrasound, the case was diagnosed as anemia with stage 3 chronic kidney disease and therapeutic interventions were initiated. The dog was reviewed at weekly intervals and was showing progressive clinical improvement in the appetite, body condition. Blood tests during reviews showed progression in hematology. The patient showed recovery from anemia after 4 consecutive treatments with Darbepoetin at weekly intervals with prevailing chronic kidney disease.

Keywords: Canine, chronic kidney disease, darbepoetin, hyperphosphatemia, anemia

Introduction
Chronic kidney disease (CKD) is defined as the presence of structural or functional abnormalities of one or both the kidneys that have been present for an extended period, usually 3 months or longer (Polzin, 2011) [4]. Dogs with CKD usually presented with loss of appetite, vomiting, lethargy, progressive weight loss and oliguria, having altered hemato-biochemical parameters viz., elevated BUN, Creatinine and Phosphorus in serum biochemistry and Anemia parallels the degree of renal impairment and its most important cause is failure of renal erythropoietin secretion. Other factors include chronic blood loss, hemolysis and bone marrow suppression by retained uremic factors (Dodds and Nicholls, 1983) [6].

Case observation and Diagnosis
A 4 years old male Labrador retriever was presented to the Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli, with a history of anorexia, lethargy, depression and weight loss. The animal was vaccinated and dewormed regularly; Clinical examination revealed dullness and depression, muscle wasting and lethargic, pale conjunctival mucous membrane, ozena and dehydration. Vitals showed increased respiratory rate and depth, tachycardia (110 bpm), increased intensity of heart sound with haemic murmurs and increased amplitude of femoral pulse with Euthermia.
Hematology (Table 1) revealed anemia (hemoglobin concentration = 4 dl; PCV = 12.1%; Erythrocyte count = 2.05 million/cmm and leucopenia (4000 /cmm). The peripheral blood smear and wet film examination revealed no blood parasites. Serum biochemistry (Table 2.1 and 2.2) revealed elevation in BUN (280.84 mg/dl), Creatinine (4.8 mg/dl), Phosphorus (6.4 mg/dl), Sodium (163.2 mg/dl) and Glucose (192 mg/dl). All other parameters were within the normal range. Abdominal ultrasound (Fig.1) revealed both the kidneys became shrunken, loss of cortico-medullary junction and abnormal echogenicity compared to other viscera. No renal calculi were evident. Bladder wall thickening with mild sludge noticed in the urinary bladder on abdominal ultrasound. Liver, Spleen and Prostate appeared with normal echogenicity. Abdominal ultrasound impressions were suggestive of severe renal damage on par with serum biochemical reports; the patient was in stage III of chronic kidney disease (Table 3) based

on IRIS, 2017 classification.

Treatment and Discussion

The animal was started with Inj. Dextrose Normal Saline @ 300 ml IV, Antibiotics – Inj. Amoxycillin @ 22 mg/kg bwt IV, Inj. Pantoprazole 1 mg/kg bwt IV, Inj. Tribivet 3 ml iv for a week and Inj. Darbepoetin (CRESP 40) @ 0.45 mcg/kg SC at weekly intervals (Fig.2) until low normal hematocrit was observed. Oral renal supplement with Rhubarb extracts (RUBENAL 300) @ 2 tablets twice daily; Phosphate binders (IPAKITINE powder 180 g) @ 12 scoops at divided doses, iron supplements (aRBCe pet 200 ml) @ 15 ml/day PO and commercial renal diet (Vet Pro) were advised. After 4 weeks of the therapeutic management, the animal was having improved appetite and physical activity. On clinical examination, the conjunctival mucous membrane turned from pale to mild pink and other vital parameters were within the normal range. Post treatment complete blood profile was obtained for hemato-biochemical evaluation. PCV is the hallmark of darbepoetin efficacy in chronic kidney disease patients. A rise in PCV of 20% and above (Table 1) suggested that darbepoetin is stimulating the Erythropoietin hormone in reviving the anemic status of the patient. The value of hematology were increased hemoglobin concentration (7.1 g/dl), increased hematocrit (20.7%) and increased erythrocyte count (3.21 million/cmm); WBC count (5500 /cmm) and thrombocyte count (3.42 lakhs/cmm) were within normal range. Serum biochemistry (Table 2.1 and 2.2) revealed no drastic change in the renal markers such as BUN (231.04 mg/dl), Creatinine (4.0 mg/dl), except phosphorus (4.3 mg/dl) which reversed to normal range.

Table 1: Hematological parameters of the dog affected with chronic kidney disease

Parameters	Before treatment	After treatment	Reference value
Hb (g/dl)	4	7.1	12-19
PCV %	12.1	20.7	37-57
RBC (M/cmm)	2.05	3.21	5-9
WBC (M/cmm)	4000	5500	5-15
Platelet (L/cmm)	3.39	3.42	1.6-5.1

Note: g/dl = gram per deciliter; % = percentage; M/cmm = million per cubic millimeter; lakh/cmm = lakhs per cubic millimeter

Table 2.1: Serum biochemical parameters of the dog affected with chronic kidney disease

BUN (mg/dl)	280.84	231.04	10-28
Creatinine (mg/dl)	4.8	4.0	0.5-1.5
Total protein (g/dl)	6.5	6.7	5.4-7.1
ALT (IU/dl)	37	31	21-102
ALP(IU/dl)	97	103	20-156
Glucose (mg/dl)	192	190	65-118

mg/dl = milligram per deciliter; g/dl = gram per deciliter; IU/dl = international units per deciliter;

Table 2.2: Serum electrolytes parameters of the dog affected with chronic kidney disease

Calcium (mmol/dl)	7.2	9.3	9-11.3
Phosphorus (mmol/dl)	6.4	4.3	2.6-6.2
Sodium (mmol/dl)	163.2	220	142-152
Pottasium (mmol/dl)	1.06	1.41	4.37-5.35

mmol/dl = millimole per deciliter

Table 3: Staging of Chronic Kidney Disease (CKD) in dogs based on IRIS, 2017 classification

	Stage of CKD	Creatinine level
1	I	1.5
2	II	1.5-2.0
3	III	2.1-5.0
4	IV	>5.0

Chronic kidney disease in canines usually presented with vomiting, lethargy, anorexia, oliguria and progressive weight loss furthermore, when anemia parallels with CKD, exercise intolerance, generalized weakness and respiratory distress are evident. In the present study, the animal had anorexia, lethargy and loss of body weight since 2 weeks of presentation. In the present case study, altered hematological parameters viz., reduced hemoglobin, packed cell volume, red blood cell counts and leukopenia indicating severe non-regenerative anemia, and altered serum biochemical parameters viz., elevated BUN, Creatinine and Phosphorus and hypokalemia indicating the presence of CKD. Hyperphosphatemia was observed along with elevated serum BUN and Creatinine in the CKD patient. A suggestive reason for hyperphosphatemia is declining kidney function because the kidneys are the primary route of phosphorus excretion and its consequences results in phosphorus retention. In chronic kidney disease, serum phosphorus concentrations typically parallel to the serum urea nitrogen concentrations and it correlated significantly with the severity of disease. Thus, hyperphosphatemia is common in azotaemia, but not in non-azotemic renal disease (Polzin, 2010) [3]. Hyperphosphatemia promotes progressive renal lesions and was found to be associated with increased morbidity and mortality in CRF dogs (Kestenbaum *et al*., 2005) [2]. Hypokalemia is also a common manifestation of CKD, that the dogs' benefit from potassium supplementation through the intravenous fluids (Polzin, 2011) [4]. The absence of haemoprotozoan diseases in peripheral blood and wet blood film examinations are passively supporting the diagnosis. The abdominal ultrasound (Fig.1) strongly suggesting the presence of severe renal damage of chronic origin viz., shrunken kidneys, loss of corico-medullary junction and altered echogenicity in comparision with other visceral organs, as chronic kidney disease is an irreversible and progressive loss of renal function, resulting from the reduced functional nephron counts.

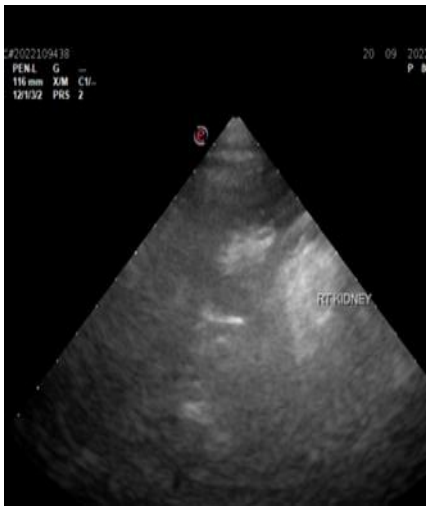

Fig 1: Shrunken right kidney on abdominal ultrasound of the Labrador retriever dog with CKD

Fig 2: Labrador retriever dog with CKD induced anemia treated with CRESP 40 injection

In advanced chronic renal disease the synthesis of Erythropoietin decreases and is insufficient to meet the demands for new red cell production, leading to anemia (Braun and Lefebvre, 2008 and Silverberg *et al.*, 2002) [9, 7]. Apart from deficiency of erythropoietin in CKD, shortened survival period of red blood cells, deficient absorption of iron, Vitamin B12 or folate deficiency, poor nutrition and spontaneous blood loss are the other causes of anemia in CKD (Kalyani Thakur *et al*. 2021) [8]. Darbepoetin alfa is a synthetic erythropoietin analog that is commonly used in human patients with CKD induced anemia (Polzin, 2013) [5]. Accordingly Baranidharan GR *et al*. 2019 concluded that Darbepoetin @ 0.5 µg/kg s/c proved safe and effective in improving packed cell volume in CKD dogs as an alternative to packed RBC or whole blood transfusion. Similarly Eporise is a man -made version of human erythropoietin that stimulates the bone marrow to produce red blood cells (Ghosh CK *et al*. 2022) [1].

With this backdrop, the present case was treated with synthetic form of erythropoietin drug Darbepoetin, which has showed improvement in the blood profile on par with physical improvement in the health of the animal. Fiocchi EH *et al*. 2017 [10] suggested achieving target PCV as a response to erythropoiesis stimulating agents (ESA), as there is no universally accepted definition for response to ESA. Our case study suggests that increase in PCV could be remarked as a positive response to Darbepoetin treatment, because PCV is a measure of proportion of blood that is made up of red blood cells. Other supportive treatments including fluid therapy to alleviate uremia; antibiotics and antacids to alleviate GI disorders, phosphate binders to alleviate hyperphosphatemia and renal diet to prevent further renal damage are simultaneously aimed for the management of chronic renal disease in the affected dog.

Conclusion

To concur, darbepoetin usage is highly significant in patients with chronic kidney disease and erythropoietin insufficiency. PCV remarks a gold standard test to choose the succeeding dose of darbepoetin in CKD patients. Use of darbepoetin in CKD is truly a supporting drug in a failing kidney towards End Stage Renal Disease (ESRD).

References

1. Ghosh CK, Mridha F, Mondal M, Guha SK, Kesh SS, Chaudhuri S, *et al*. Ameliorative effect of hemodialysis in a dog having chronic kidney disease. The Pharma Innovation Journal. 2022;SP-11(6):904-907.
2. Kestenbaum B, Sampson JN, Rudser KD, Patterson DJ, Seliger SL, Young B, *et al*. Serum phosphate levels and mortality risk among people with chronic kidney disease. Journal of American Society of Nephrology. 2005;16(2):520-528.
3. Polzin DJ. Chronic kidney disease. In: Ettinger SJ, Feldman EC, editors, Textbook of veterinary internal medicine, St Louis (MO): Saunders Elsevier. 2010;2:1990-2021.
4. Polzin DJ. Chronic Kidney disease in small animals. Vet Clin North Am Small Anim Pract. 2011;41:15-30.
5. Polzin D. Evidence-based step-wise approach to managing chronic kidney disease in dogs and cats. J Vet Emerg Crit Care. 2013;23:205-215.
6. Dodds A, Nicholls M. Haematological aspects of renal disease. Pub Med – index for medline. 1983;11(4):361-368.
7. Silverberg DS, Wexler D, Blum M. The correction of anemia in severe resistant heart failure with erythropoietin and intravenous iron prevents the progression of both the heart and the renal failure and markedly reduces hospitalization. Clinical Nephrology. 2002;58(1):37-45.
8. Kalyani Thakur, Dhoot VM, Bhojne GR, Upadhye SV. Intermittent hemodialysis in a labrador retriever dog. The Pharma Innovation Journal. 2021;SP-10(7):689-693.
9. Braun JP, Lefebvre HP. Kidney Function and Damage In: Clinical Biochemistry of Domestic Animals, 6th Edition, Elsevier Inc, 2008, 485-528. doi: 10.1016/B978-0-12-370491-7.00016-7
10. Fiocchi EH, Cowgill LD, Brown DC, Markovich JE, Tucker S, Labato MA, *et al*. The Use of Darbepoetin to Stimulate Erythropoiesis in the Treatment of Anemia of Chronic Kidney Disease in Dogs. J Vet Intern Med 2017;31:476-485.