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Short Communication

IMPACT OF DARBOPOIETIN IN ANEMIC DOGS WITH CHRONIC KIDNEY DISEASE

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SUMMARY

The aim of the study was to assess the efficacy of darbopoietin in the treatment of chronic kidney diseases induced anemia in dogs. Chronic kidney diseases in dogs were diagnosed on the basis of clinical manifestation, haemogram, serum biochemistry, urine analysis and ultrasonogram. In the present study, the structural and functional losses of kidneys were assessed by ultrasonography and treatment was given to the affected dogs to prevent further damage. Severe anemia reported in present study is a consequence of the chronic kidney disease which may lead to poor prognosis. Darbopoietin @0.6 microgram per kg body weight was administered subcutaneously every week for four weeks and tapered to once in two weeks to induce the erythropoiesis. After the treatment protocol, the dogs showed increased hemogram values in turn helped to prolong the life of the animals.

Keywords: Anemia, Chronic Kidney Disease, Darbopoietin, Dog

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Erythropoietin is a hormone synthesized by the kidneys which induces erythropoiesis. In chronic kidney disease (CKD), an abnormal change occurs in structure and functions of the kidneys which in turn may affect erythropoietin synthesis resulting in anemia (Cases *et al.*, 2018 and Lippi *et al.*, 2021). As per the reports of several authors, anemia is a major complication of CKD patients (Cases *et al.*, 2018 and Lippi *et al.*, 2021). Erythropoiesis-stimulating agents (ESAs) are endogenous glycoprotein hormones which stimulate erythropoiesis by similar mechanism as erythropoietin (MacDougall, 2008 and Walter, 2013). Recent research recommends ESAs for the treatment of CKD induced anemia (Walter, 2013 and Fiocchi *et al.*, 2017) and these reduced the clinical complications due to anemia which may improve longevity of the CKD patients (Fiocchi *et al.*, 2017). Darbepoetinalfa is a synthetic compound with high molecular weight that leads to three fold increase in half-life resulting in higher *in vivo* potency than recombinant human erythropoietin (rHuEPO) (Feriani *et al.*, 2011 and Fiocchi *et al.*, 2017). Therefore, the present study was undertaken to assess the efficacy of darbopoietin in alleviating chronic kidney disease induced anemia in dogs.

The dogs were randomly selected based on the history and age which were brought to Small Animal Medicine Unit, Veterinary Clinical Complex, Rajiv Gandhi Institute of Veterinary Education and Research, Puducherry; with clinical signs suggestive of chronic kidney disease like anorexia, progressive loss in weight, polyuria, polydipsia, vomiting, pale to blanched mucus membrane and melena. Blood samples collected from the saphenous/femoral vein were subjected to haemoto-biochemistry examination as per the standard methods (Schalm *et al.*, 2000). Urine samples were obtained by cystocentesis, catheterization or natural void and subjected to physical, chemical and microscopic examination (Coles, 1986). Ultrasonographic examination was carried out as per the procedures described by Nyland *et al.* (2005). Dogs suffering from chronic kidney disease with International Renal Interest Society (IRIS) stages 2, 3 and 4 were included under the study. A group of six animals with chronic kidney disease having PCV less than 35 percent and haemoglobin below 12 g/dl was considered as anemic dogs and was treated with Inj. Darbopoietin @ 0.6 µg/kg body weight sub-cutaneously every week for four weeks and tapered to once in two weeks. The parameters in the study were evaluated on the day 0 and after four weeks for the efficacy of the drug. Dogs were treated for CKD with Inj. Enrofloxcin @ 7.5 mg/kg body weight intramuscular route for ten days, Inj. Chlorpheniramine maleate @ 0.2mg/kg body weight, Syp. Advaren @ 10ml BID orally and Cap. Renodyl 1tab TID orally for one month as enteric dialysis. The haematological and serum biochemistry values, before and after treatment were subjected to paired t test to the study statistically significance of the drug (Snedecor and Cochran, 1989).

Efficacy of darbopoietin was evaluated by pre-treatment and post-treatment through anamnesis, clinical signs, haematology, serum biochemistry, urine analysis and ultrasonogram. The mean haemogram and serum biochemistry of dogs with CKD before and after treatment are given in Table 1 and Table 2.Darbopoietin has made a huge impact in the treatment of anemia of renal disease in

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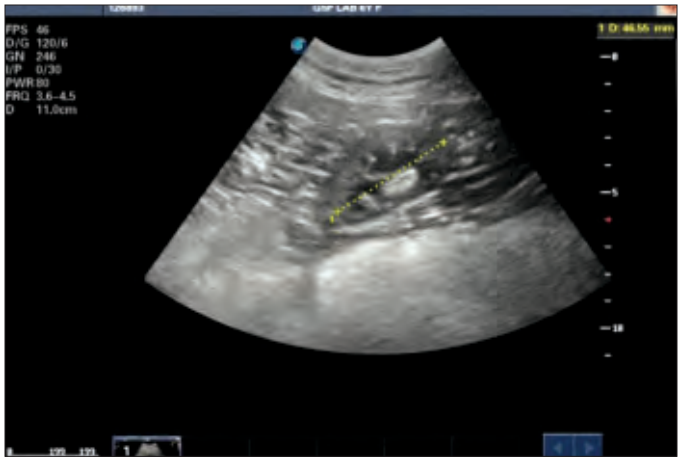

Fig. 1. Ultrasonogram of dog kidney showing atrophic changes in CKD

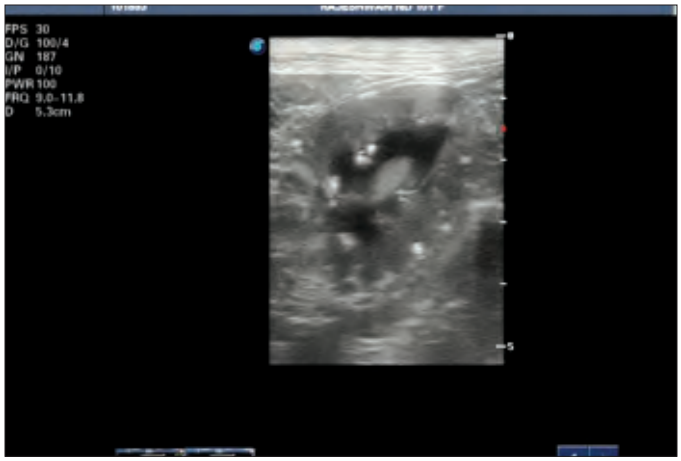

Fig. 2. Ultrasonogram of dog kidney showing thickened cortex, irregular contour and increased echogenicity of cortex and medulla in CKD

Table 1

Impact of darbopoietin on haematological parameters in dogs suffering from chronic kidney disease

S.No.	Parameters	Mean±SD Values of CKD dogs		t test
		Before Treatment (0 day)	After treatment (30th day)	
1.	Haemoglobin (g/dl)	7.8±2.0	12.1±2.4	0.000**
2.	Packed cell volume (%)	21.1±5.6	33.5±7.8	0.000**
3.	Total erythrocyte count (x106 cells/cmm)	3.3±0.9	5.4±1.1	0.000**
4.	MCV (fL)	63.5±4.8	62.0±4.3	0.386 NS
5.	MCH (pg)	23.3±1.6	22.4±1.6	0.324 NS
6.	MCHC (%)	36.7±1.3	36.2±2.0	0.656 NS
7.	Total leucocyte count (x103 cells/cmm)	12737±5660.0	8710±1491.8	0.037*
8.	Platelets ($x10^3$ cells/cmm)	1.7±1.1	3.2±0.7	0.001**
9.	Neutrophils (%)	76.5±9.4	74.2±2.7	0.39NS
10.	Lymphocyte (%)	17.6±8.4	23.8±2.6	0.030*
11.	Eosinophil (%)	2.1±2.6	0.6±0.7	0.134NS
12.	Monocyte (%)	3.8±3.1	1.4±1.2	0.019*

**Significant (P<0.01), * Significant (P<0.05), NS-Not significant (P>0.05)

Table 2

Impact of darbopoietin on serum biochemistry values in dogs suffering from chronic kidney disease

S.No.	Parameters	Mean±SD Values of CKD dogs		t test
		Before Treatment (0 day)	After treatment (30th day)	
1	Total protein (g/dl)	6.8±0.7	6.3±0.7	0.065*
2	Albumin (g/dl)	2.7±0.5	3.6±0.8	0.025**
3	Globulin (g/dl)	4.1±0.9	2.5±0.5	0.000**
4	Albumin/ Globulin	0.7±0.2	1.5±0.5	0.001**
5	BUN (mg/dl)	88.0±27.8	69.3±19.8	0.002**
6	Creatinine (mg/dl)	6.5±5.1	4.3±3.2	0.006**
7	Phosphorus (mg/dl)	10.9±1.4	8.6±1.6	0.009**
8	Calcium (mg/dl)	11.2±2.8	10.4±1.1	0.374NS

**Significant (P<0.01), * Significant (P<0.05), NS-Not significant (P>0.05)

cats (Chalhoub *et al.*, 2012) which is in agreement with the present study. Walter (2013) concluded that total iron binding capacity plays an important role on both anemia and erythropoiesis response to darbepoetin alfa in CKD dogs. Bartges (2012) reported a progressive normocytic normochromic anemia that is a characteristic feature of

CKD in dogs and cats which is in accordance with the present study. Darbopoietin is a analog of erythropoietin, and is a synthetic glycoprotein having three fold increased half life and acts on the erythroid progenitor cells in the bone marrow and induces the erythropoisis, which results in the increased production of blood cells. Darbopoietin effectively and significantly increased ($P<0.01$) the Hb, PCV, TEC and platelets count within 30 days in the present study which is in agreement with the results of Fiocchi *et al.*, 2017. The CKD dogs were treated with Inj. Enrofloxcin which is an ideal antibiotic that concentrates and excretes through kidney. Syp. Advaren is a herbal renoprotective preparation that acts as a diuretics, strengthens and protects kidney and improves the kidney function. Therapeutic probiotic microbes in the renodyl capsule will grow and multiply in the small intestine and consume more nitrogenous waste and effectively reduce the uremic nitrogenous waste and the metabolized toxins are eliminated from the body as solid waste (bowel) by the peristalsis movement of the intestine, thus it reduce the burden on the compromised kidneys. The fructo-oligosaccharides will maintain the gut health by supporting the growth of the healthy bacteria in the intestine. Thus, it act as a natural enteric dialysis, helps to slow down uremic toxin build up in CKD patients. CKD treatment and darbopoietin effectively and significantly increased ($P<0.01$) the mean serum albumin and albumin globulin ratio and significantly reduced ($P<0.01$) the mean serum values of globulin, BUN, creatinine, phosphorus and total protein ($P<0.05$). Urine analysis showed slight improvement in the colour and mean specific gravity (1.03) and microscopic examination revealed presence of few neutrophils, epithelial cells and absence of red blood cells as compared to pre-treatment. Chemical examination of urine showed traces of protein, glucose and ketone bodies in CKD dogs as compared to pre-treatment. Ultrasonogram of dogs with CKD showed no structural changes in pre and post- treatment. The major abnormality recorded in chronic kidney disease dogs were atropy (66%) or hypertrophy (33%) of kidney size (Fig. 1), irregular renal countour (83%), indistinct cortico medullary junction (83%), medullary ring sign (33%), increased cortical echogenicity and cortical thickening (100%) and increased medullary echogenicity (66%) as shown in Fig. 2.

Fiocchi *et al.*, 2017 concluded that, an effective dose rate of darbopoietin in the treatment of anemic CKD dogs was 0.8 microgram per kg body weight subcutaneously to attain the target PCV which in turn increase the survival time to 162 days. Based on the above analysis, darbopoietin was chosen as an ideal drug of choice against CKD induced anemia in dogs. In the present study, effective dose rate was 0.6 µg/kg body weight subcutaneously every week for four weeks and tapered to once in two weeks to raise the target PCV and clinically there was no adverse effect recorded but Fiocchi *et al.* (2017) recorded the common adverse effects of darbopoietin as increased systolic blood pressure, hyperkalemia, thrombocytosis, seizures, diarrhea, vomiting and red cell aplasia. The given treatment effectively reduced the clinical signs and improved the body condition, appetite, recovery from lethargy, pale to blanched mucosa and melena in anemic CKD dogs. Early detection of the chronic kidney disease, prompt therapy and supportive treatment like darbopoietin will reduce the risk and increase the life span of the animals.

REFERENCES

Bartges, J.W. (2012). Chronic kidney disease in dogs and cats. *Vet. Clin. North Am. Small Anim. Pract.* **42**: 669–692.

Cases, A., Egocheaga, M.I., Tranche, S., Pallares, V., Ojeda, R., Gorriz, J.L. and Portoles, J.M. (2018). Anemia of chronic kidney disease: Protocol of study, management and referral to nephrology. *Nefrologia.* **38**: 8–12.

Chalhoub, S., Langston, C. and Farrelly, J. (2012). The use of darbepoetin to stimulate erythropoiesis in anemia of chronic kidney disease in cats: 25 cases. *J. Vet. Intern. Med.* **26**: 363–369.

Coles, E.H. (1986). Veterinary Clinical pathology (4th Edn.) Philadelphia, W.B. Saunders Co., U.S.A. pp. 171-202.

Feriani, M., De Meester, J.M.J., McMahon, L.P., Rottembourg, J.B., Bridges, I., Farouk, M. and Pronai, W. (2011). Extended dosing of darbepoetin alfa in peritoneal dialysis patients. *BMC. Nephrology.* **12(1)**: 13.

Fiocchi, E.H., Cowgill, L.D., Brown, D.C., Markovich, J.E., Tucker, S., Labato, M.A. and Callan, M.B. (2017). The use of Darbepoetin to stimulate erythropoiesis in the treatment of anemia of chronic kidney disease in dogs. *J. Vet. Intern. Med.* **31(2)**: 476-485.

Lippi. I., Perondi, F., Lubas, G., Gori, E., Pierini, A., D'Addetta, A. and Marchetti, V. (2021). Erythrogram patterns in dogs with chronic kidney disease. *Vet. Sci.* **8(7)**: 123.

MacDougall, I. (2008). Novel erythropoiesis-stimulating agents: A new era in anemia management. *Clin. J. Am. Soc. Nephrol.* **3**: 200-207.

Nyland, T.G., Park, R.D., Lattimer, J.C. and Miller, C.W. (2005). Gray scale ultrasonography of the canine abdomen. *Vet. Radiol. Ultrasound.* **22(5)**: 220-227.

Schalm, O.W., Weiss Douglas, J. and Wardrop, K.J. (2000). Veterinary Haematology (6th Edn.), Wiley Blackwell publishing, U.S.A. pp. 799-809.

Snedecor, G.W. and Cochran, W.G. (1989). Statistical methods (8th Edn.), Iowa state university press, USA.

Walter, H.H. (2013). Differentiating factors between erythropoiesis-stimulating agents: An update to selection for anaemia of Chronic Kidney Disease. *Drugs.* **73**: 117–130.