



Muscle Weakness and Hyporeflexia; is Diabetic Neuropathy the Culprit?

Kerem Ural¹, İbrahim Akın², Canberk Balıkcı¹, Ümit Karademir³, Songül Toplu¹

¹Adnan Menderes University, Faculty of Veterinary, Department of Internal Medicine, Isikli, Aydin, TURKEY

²Adnan Menderes University, Faculty of Veterinary, Department of Surgery, Isikli, Aydin, TURKEY

³Adnan Menderes University, Faculty of Veterinary, Department of Pharmacology and Toxicology, Isikli, Aydin, TURKEY

Correspondence to: Kerem URAL, Adnan Menderes Üniversitesi, Veteriner Fakültesi, İç Hastalıkları Anabilim Dalı, Işıklı, Aydın, Türkiye. E-mail: uralkerem@gmail.com

Diabetic neuropathy (DNeur) is not frequently seen in dogs. Primary clinical findings in dogs involve chronic and progressive hindlimb weakness, probably extending to occur within the forelimbs (Morgan et al., 2008; Schaer, 2010). Actually the real incidence of peripheral neuropathy (PN) presenting in dogs with diabetes mellitus (DM) remains unclear (Morgan et al., 2008). Prior researches regarding canine diabetic neuropathy (DNeur) might be classified to those of dogs with subclinical PN (Steiss et al., 1981; Braund and Steiss, 1982; Sharma et al., 1995; Ghani et al., 1999; Walker et al., 2001), and to those of which dogs with clinical signs of PN (Anderson et al., 1983; Johnson et al., 1983; Katherman and Braund, 1983). In several studies including dogs with spontaneous or experimental DNeur, presenting no neurological signs, diagnosis was based on histopathologic or electrodiagnostic findings (Steiss et al., 1981; Braund and Steiss, 1982; Sharma et al., 1995; Ghani et al., 1999; Walker et al., 2001). Contrarily clinical signs of PN associated with spontaneous DM was described among 4 different studies (Anderson et al., 1983; Johnson et al., 1983; Katherman and Braund, 1983).



Figure 1. Clinical appearance of a dog with DNeur. At physical examination a) a profound muscle weakness, c-d) hyporeflexia, and hypotonia were evident. Left forelimb was affected, in which the dog was unvoluntarily walking. Following 6 months of treatment e) the dog was presenting better locomotor activity.

Şekil 1. Diyabetik nöropatili köpeğin klinik görünümü. Fiziksel muayenede a) belirgin bir kas zafiyet, c-d)hiporefleksi ve hipotoni mevcuttu. Sol ön ayak etkilenmiş, olgu gönülsüz olarak yürümekteydi. Sağaltımı takiben 6. ayda e) köpeğin daha iyi bir lokomotor aktiviteye sahip olduğu gözlemlenmekte.

The diagnosis of a PN is supported by clinical signs, nerve biopsies, and muscle biopsies, besides by electromyographic examination (Cuddon, 2002; Inzana, 2005). As was also aforementioned above clinical signs suggestive of a PN include muscle atrophy/weakness, hyporeflexia, and hypotonia (Munana, 1995; Cuddon, 2002; Inzana, 2005).

Table 1. Serum biochemical analysis of a 7 years old male dog with DNeur receiving alpha lipoic acid.
Tablo 1. Alfa lipoik asit uygulanan Diabetik nöropatili 7 yaşlı erkek köpekte serum biyokimyasal analiz sonuçları.

Test (mg/L) (reference interval)	Fructosamine (μ mol/L)	HbA1c (%)	Glucose (mg/dL)
Day 0	540	7.8	376
6 months later	475	6.4	230

An 6-years-old, intact male, crossbred dog was examined at the University of Adnan Menderes, Faculty of Veterinary Veterinary, Department of Internal Medicine, for a 7-months history of limb weakness, with waxing and waning signs. While standing (Figure 1 a-d) and walking, the affected limb was less prone to weight bearing. The affected limb was thinner and smaller width than other, relatively. During walking moderate/severe lameness was observed. The dog had a 2,5-years history of DM, which was being treated with Humulin-R (human recombinant) and first occasion, and afterwards by Humulin-N [neutral protamine Hagedorn (NPH) insulin] by private veterinary practice. On admission to our clinic serial blood glucose measurements, glycolized haemoglobin-HbA1c and fructosamine (Table 1) were analyzed. The owner was instructed to alternate the dose for insulin preparation, besides especially forced for usage of alpha lipoic acid (Thioctacid 600 HR, 600 mg, Meda Pharma GmbH, Germany) at a dose of 50 mg/kg (Paetau-Robinson et al., 2013) for 6 months.

Following 6 months of treatment the dog was otherwise healthy and muscle weakness was disappeared (Fig. 1e). It was observed that metabolic panel values was better than the initial submission (Table 1). Alpha lipoic acid has been extensively tested for its efficacy in human medicine against diabetic polyneuropathy to several other diseases (Grunert, 1960; Baur et al., 1991; Packer et al., 1995; Wenzel et al., 2005; Yadav et al., 2005; Ziegler et al., 2006; Holmquist et al., 2007; Sehirlir et al., 2008). Furthermore it has been recommended for treatment of different diseases in veterinary field [i.e. DM, DNeur (Wynn and Marsden, 2003; Means, 2008) cataracts and glaucoma (Wynn and Marsden, 2003). In the present study the latter compound resulted with glucose lowering effects, and to the present authors' knowledge prevented the development of the condition. More detailed clinical studies are further warranted in an attempt to understand the efficacy of alpha lipoic acid for treatment of DNeur in dogs.

References

- Anderson PG, Braund KG, Dillon AR, Sartin JL (1983). Polyneuropathy and hormone profiles in a chow puppy with hypoplasia of the islets of langerhans. *Veterinary Pathology*, 23, 528–531.
- Baur A, Harrer T, Peukert M, Jahn G, Kalden JR and Fleckenstein B (1991). Alpha-lipoic acid is an effective inhibitor of human immunodeficiency virus (HIV-1) replication. *Wiener klinische Wochenschrift*, 69, 722–724.
- Braund KG and Steiss JE (1982). Distal neuropathy in spontaneous diabetes mellitus in the dog. *Acta Neuropathol (Berl)*, 57, 263–269.
- Cudon PA (2002). Acquired peripheral neuropathies. *Veterinary Clinics of North American Small Animal Practice*, 32, 207–249.
- Ghani M, Malik RA, Walker D, Sharma AK, Lowrie CT, Schall WD and Boulton AJ (1999). Perineural abnormalities in the spontaneously diabetic dog. *Acta Neuropathologica (Berl)*, 97, 98–102.
- Grunert RR (1960). The effect of DL-a-lipoic acid on heavy-metal intoxication in mice and dogs. *Archives of Biochemistry and Biophysics*, 86, 190–194.
- Holmquist L, Stuchbury G, Berbaum K, Muscat S, Young S, Hager K and Münch G (2007). Lipoic acid as a novel treatment for Alzheimer's disease and related dementias. *Pharmacology & Therapeutics*, 113, 154–164.
- Inzana KD (2005). Peripheral nerve disorders. In: Ettinger SJ, Feldman EC, editors. *Textbook of Veterinary Internal Medicine*. 6. St. Louis: Elsevier Saunders; 2005. pp. 888–900.
- Johnson CA, Kittleson MD and Indrieri RJ (1983). Peripheral neuropathy and hypotension in a diabetic dog. *Journal of American Veterinary Medical Association*, 183, 1007–1009.
- Katherman AE and Braund KG (1983). Polyneuropathy associated with diabetes mellitus in a dog. *Journal of American Veterinary Medical Association*, 182, 522–524.
- Means C (2008). Ataxia and vomiting in a German Shepherd. *NAVC Clinician's Brief*, 6 (9), 31–33.
- Misselbrook NG (1987). Peripheral neuropathy in diabetic bitch (letter). *Veterinary Record*, 121, 287.
- Morgan MJ, Vite CH, Radhakrishnan A and Hess RS (2008). Clinical peripheral neuropathy associated with diabetes mellitus in 3 dogs. *The Canadian Veterinary Journal*, 49 (6), 583.
- Munana KR (1995). Long term complications of diabetes mellitus, part 1: retinopathy, nephropathy, neuropathy. *Veterinary Clinics of North American Small Animal Practice*, 25, 715–730.
- Packer L, Witt EH and Tritschler HJ (1995). Alpha-lipoic acid as a biological antioxidant. *Free Radical Biology and Medicine*, 19, 227–250.
- Paetau-Robinson I, Brejda JJ and Zicker SC (2013). Long-Term Feeding of DL- α Lipoic Acid to Dogs Is Safe. *The Journal of Applied Research in Veterinary Medicine*, 11 (2), 100–109.
- Schaer M (2010). Diabetic Neuropathy in Dogs. *NAVC Clinician's Brief Clinical View*, 56.
- Sehirlir O, Sener E, Centinel S, Yüksel M, Gedik N and Şener G (2008). a-Lipoic acid protects against renal ischaemia-reperfusion injury in rats. *Clinical and Experimental Pharmacology and Physiology*, 35, 249–255.
- Sharma AK, Malik RA, Dhar P, Mehra RD, Ahmed I, Lowrie CT and Schall WD (1995). Peripheral nerve abnormalities in the spontaneously diabetic dog. *International Journal of Diabetes in Developing Countries*, 3, 130–139.
- Steiss JE, Orsher AN and Bowen JM (1981). Electrodiagnostic analysis of peripheral neuropathy in dogs with diabetes mellitus. *American Journal of Veterinary Research*, 42, 2061–2064.
- Walker D, Siddique I, Anderson H, Gardiner TA, Archer DB, Boulton AJM and Malik RA (2001). Nerve pathology in the type 1 diabetic dog: effects of treatment with sulindac. *Journal of Peripheral Nervous System*, 6, 219–226.
- Wenzel U, Nickel A and Daniel H (2005). a-lipoic acid induces apoptosis in human colon cancer cells by increasing mitochondrial respiration with a concomitant O₂ generation. *Apoptosis*, 10, 359–368.
- Wynn SG and Marsden S (2003). *Manual of Natural Veterinary Medicine*, 2nd edn. St Louis: Mosby Inc. pp. 236, 480, 500, 510, 511.
- Yadav V, Marracci G, Lovera J, Woodward W, Bogardus K, Marquardt W and Bourdette D (2005). Lipoic acid in multiple sclerosis: a pilot study. *Multiple Sclerosis*, 11, 159–165.
- Ziegler D, Ametov A, Barinov A, Dyck PJ, Gurieva I, Low PA and Samigullin R (2006). Oral treatment with a-lipoic acid improves symptomatic diabetic polyneuropathy. *Diabetes Care*, 29 (11), 2365–2370.