

Evaluation of epidemiological and clinical findings of canine hyperadrenocorticism in Iran

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Abstract

Hyperadrenocorticism (HAC), also known as Cushing's syndrome, is caused by chronic exposure to excessive glucocorticoids. The objective of this study was to determine the epidemiological and clinical (especially ophthalmic) findings of dogs with HAC to increase recognition of suspicious cases in clinical routines. This study was examined on thirty dogs from Tehran, Mazandaran, and Guilan provinces between April 2021 and May 2022. The dogs included in the current study, who all had confirmed Hyperadrenocorticism, were selected based on the clinical findings suggestive Cushing disease as well as positive low-dose dexamethasone-suppression test. Then, general information, clinical signs, and ophthalmic factors were examined and recorded. The data were analyzed using the Chi-square test, Fisher's exact test, McNemar test, independent samples t-test, one-way ANOVA and LSD post hoc test. The mean age for the dogs with HAC was 9.7 years. The risk of HAC was also higher in neutered than intact dogs and also in terrier breed than other ones. Furthermore, significant differences were statistically observed concerning ophthalmic evaluations, including eye lesions, palpebral reflex, ophthalmic structural disorders, conjunctival, sclera, lens, retina, iris, and optic nerve involvement. However, gender, breed, common clinical manifestations, behavioural status, PLR test, menace test, dazzle test, cotton test, and corneal involvement did not show significant differences statistically. It was concluded that indoor and gonadectomized dogs had higher frequency in the studied population. We conducted epidemiological and clinical study of Cushing's disease in dogs in Iran, and for the first time, we examined the eye factors associated with this syndrome. These results support a better understanding of the canine hyperadrenocorticism in Iran. According to this study, the studied population resembles the profile described in European and North American epidemiologic studies, and the clinical picture of the HAC dog appears to be similar worldwide.

Key words: Polyuria, Polydipsia, Hyperadrenocorticism, Dog, Eye

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References

- Barker, E. N., Campbell, S., Tebb, A. J., Neiger, R., Herrtage, M. E., Reid, S. W., & Ramsey, I. K. (2005). A comparison of the survival times of dogs treated with mitotane or trilostane for pituitary-dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine*, 19(6): 810-815.
- Behrend, E.N. (2015). *Canine and feline endocrinology* (4th ed., pp. 377-444). St Louis, SL: W.B. Saunders.
- Behrend, E. N., Kooistra, H. S., Nelson, R., Reusch, C. E., & Scott-Moncrieff, J. C. (2013). Diagnosis of spontaneous canine hyperadrenocorticism: 2012 ACVIM consensus statement (small animal). *Journal of Veterinary Internal Medicine*, 27(6): 1292-1304.
- Belanger, J. M., Bellumori, T. P., Bannasch, D. L., Famula, T. R., & Oberbauer, A. M. (2017). Correlation of neuter status and expression of heritable disorders. *Canine Genetics and Epidemiology*, 4(1): 6.
- Bell, R., Neiger, R., McGrotty, Y., & Ramsey, I. K. (2006). Study of the effects of once daily doses of trilostane on cortisol concentrations and responsiveness to adrenocorticotrophic hormone in hyperadrenocorticoid dogs. *The Veterinary Record*, 159(9): 277-281.
- Benckroun, G., de Fornel-Thibaud, P., Rodríguez Piñeiro, M. I., Rault, D., Besso, J., Cohen, A., Hernandez, J., Stambouli, F., Gomes, E., Garnier, F., Begon, D., Maurey-Guenec C., & Rosenberg, D. (2010). Ultrasonography criteria for differentiating ACTH-dependency from ACTH independency in 47 dogs with hyperadrenocorticism and equivocal adrenal asymmetry. *Journal of Veterinary Internal Medicine*, 24(5): 1077-1085.
- Burkhardt, W. A., Boretti, F. S., Reusch, C. E., & Sieber-Ruckstuhl, N. S. (2013). Evaluation of baseline cortisol, endogenous ACTH, and cortisol/ACTH ratio to monitor trilostane treatment in dogs with pituitary-dependent hypercortisolism. *Journal of Veterinary Internal Medicine*, 27(4): 919-923.
- Carotenuto, G., Malerba, E., Dolfini, C., Brugnoli, F., Giannuzzi, P., Semprini, G., & Fracassi, F. (2019). Cushing's syndrome an epidemiological study based on a canine population of 21,281 dogs. *Open Veterinary Journal*, 9(1): 27-32.
- Castillo, V. A., Pessina, P. P., Garcia, J. D., Hall, P., Gallelli, M. F., Miceli, D. D. & Cabrera Blatter, M. F. (2014). Ectopic ACTH syndrome in a dog with a mesenteric neuroendocrine tumour: a case report. *Veterinary Medicina*, 59(7): 352-358.
- Da Silva, C. C., Cavalcante, I., de Carvalho, G. L. C. & Pöppel, Á. G. (2021). Cognitive dysfunction severity evaluation in dogs with naturally-occurring Cushing's syndrome: A matched case-control study. *Journal of Veterinary Behavior*, 46: 74-78.
- Fracassi, F., Corradini, S., Floriano, D., Boari, A., Aste, G., Pietra, M., Bergamini, P. F. & Dondi, F. (2015). Prognostic factors for survival in dogs with pituitary-dependent hypercortisolism treated with trilostane. *The Veterinary Record*, 176(2): 49-55.
- Galac, S. (2010). Recent developments in canine Cushing's syndrome. Utrecht Universiteit Utrecht, Faculteit Diergeneeskunde Thesis Universiteit Utrecht. - With ref. - With summary in Dutch and Slovene. 1, 978.
- Gallelli, M. F., Cabrera M. F. B. & Castillo V. (2010). A comparative study by age and gender of the pituitary adenoma and ACTH and alpha-MSH secretion in dogs with pituitary-dependent hyperadrenocorticism. *Research in Veterinary Science*, 88(1): 33-40.
- Gilor, C. & Graves T. K. (2011). Interpretation of laboratory test for canine Cushing's syndrome. *Topics in Companion Animal Medicine*, 26(2): 98-108.
- Hanson, J. M., Teske, E., Voorhout, G., Galac, S., Kooistra, H. S. & Meij, B. P. (2007). Prognostic factors for outcome after transsphenoidal hypophysectomy in dogs with pituitary-dependent hyperadrenocorticism. *Journal of Neurosurgery*, 107(4): 830-840.
- Helm, J. R., Mclachlan, G., Boden, L. A., Frowde, P. E., Collings, A. J., Tebb, A. J., Elwood, C. M., Herrtage, M. E., Parkin, T. D. & Ramsey, I. K. (2011). A comparison of factors that influence survival in dogs with adrenal-dependent hyperadrenocorticism treated with mitotane or trilostane. *Journal of Veterinary Internal Medicine*, 25(2): 251-260.
- Koestel, Z. L., Backus R. C., Tsuruta, K., Spollen, W. G., Johnson S. A., Javurek, A. B., Ellersieck, M. R., Wiedmeyer, C. E., Kannan, K., Xue, J., Bivens, N. J., Givan, S. A. & Rosenfeld, C. S. (2017). Bisphenol A (BPA) in the serum of pet dogs following short-term consumption of canned dog food and potential healthconsequences of exposure to BPA. *The Science of the Total Environment*, 579: 1804-1814.

- Lane, IF., Roberts, S. T. & Lappin, M. R. (1993). Ocular manifestations of vascular disease: Hypertension, hyperviscosity, and hyperlipidemia. *Journal of American Animal Hospital Association*, 29: 28-36.
- Maggs, D. J., Miller, P., & Ofri, R. (2016). *Slatter's Fundamentals of Veterinary Ophthalmology* (6th ed., pp. 79-109). St Louis, SL: W.B. Saunders.
- Martins, F. S., Carvalho, G. L. C., Jesus, L., Pöpl, Á. G., & González, F. H. (2019). Epidemiological, clinical, and laboratory aspects in a case series of canine hyperadrenocorticism: 115 cases (2010-2014). *Pesquisa Veterinária Brasileira*, 39(11): 900-908.
- Midzak, A. & Papadopoulos, V. (2016). Adrenal mitochondria and steroidogenesis: from individual proteins to functional protein assemblies. *Frontiers in Endocrinology*, 7: 106.
- Nelson, R. W. and Couto, C. G. (2020). *Small Animal Internal Medicine* (6th ed., pp. 857-897). St Louis, SL: Elsevier.
- Notari, L., Burman, O. & Mills, D. S. (2016). Is there a link between treatments with exogenous corticosteroids and dog behavior problems?. *The Veterinary Record*, 179(18): 462-467.
- O'Neill, D. G., Scudder, C., Faire, J. M., Church, D. B., McGreevy, P. D., Thomson, P. C. & Brodbelt, D. C. (2016). Epidemiology of hyperadrenocorticism among 210,824 dogs attending primary-care veterinary practices in the UK from 2009 to 2014. *The Journal of Small Animal Practice*, 57(7): 365-373.
- Peterson, M. E. (2007). Diagnosis of hyperadrenocorticism in dogs. *Clinical Techniques in Small Animal Practice*, 22(1): 2-11.
- Plassais, J., Rimbault M., Williams F. J., Davis B.W., Schoenebeck J. J. & Ostrander E. A. (2017). Analysis of large versus small dogs reveals three genes on the canine X chromosome associated with body weight, muscling and back fat thickness. *PLoS Genetics*, 13(3), e1006661.
- Pöpl, A. G., Coelho, I. C., Silveira, C. A., Moresco, M. B., & Carvalho, G. L. C. (2016). Frequency of endocrinopathies and characteristics of affected dogs and cats in southern Brazil (2004-2014). *Acta Scientiae Veterinariae*, 44(1): 1379.
- Reusch, C. E., & Feldman, E. C. (1991). Canine hyperadrenocorticism due to adrenocortical neoplasia: pretreatment evaluation of 41 dogs. *Journal of Veterinary Internal Medicine*, 5(1): 3-10.
- Rodriguez Piñeiro, M. I., De Fornel-Thibaud, P., Benckekroun, G., Garnier, F., Maurey-Guenec, C., Delisle, F., & Rosenberg, D. (2011). Use of computed tomography adrenal gland measurement for differentiating ACTH dependence from ACTH independence in 64 dogs with hyperadrenocorticism. *Journal of Veterinary Internal Medicine*, 25(5): 1066-1074.
- Van der Woerd, A. & Peterson, M. E. (2000). Prevalence of ocular abnormalities in cats with hyperthyroidism. *Journal of Veterinary Internal Medicine*, 14(2): 202-203.
- Van Rijn, S. J., Galac, S., Tryfonidou, M. A., Hesselink, J. W., Penning, L. C., Kooistra, H. S., & Meij, B. P. (2016). The influence of pituitary size on outcome after transsphenoidal hypophysectomy in a large cohort of dogs with pituitary-dependent hypercortisolism. *Journal of Veterinary Internal Medicine*, 30(4): 989-995.
- Van Rijn, S. J., Hanson, J. M., Zierikzee, D., Kooistra, H. S., Penning, L. C., Tryfonidou, M.A., & Meij, B. P. (2015). The prognostic value of perioperative profiles of ACTH and cortisol for recurrence after transsphenoidal hypophysectomy in dogs with corticotroph adenomas. *Journal of Veterinary Internal Medicine*, 29(3): 869-876.
- Wang, Y., Brûlé, E., Silander, T., Bak, B., Joustra, S. D., & Bernard D. J. (2017). The short mRNA isoform of the immunoglobulin superfamily, member 1 gene encodes an intracellular glycoprotein. *PLoS One*, 12(7): e0180731.
- Wood, F. D., Pollard, R. E., Uerling, M. R. Feldman, E.C. (2007). Diagnostic imaging findings and endocrine test results in dogs with pituitary-dependent hyperadrenocorticism that did or did not have neurologic abnormalities: 157 cases (1989–2005). *Journal of the American Veterinary Medical Association*, 231(7): 1081-1085.
- Wooten, K. J., & Smith, P. N. (2013). Canine toys and training devices as sources of exposure to phthalates and bisphenol A: quantitation of chemicals in leachate and in vitro screening for endocrine activity. *Chemosphere*, 93(10): 2245-2253.