

# Successful management of hypoadrenocorticism in a French Bulldog by a smaller dose and lesser frequency of the desoxycorticosterone pivalate: a case report

Phuttiapan Channgam<sup>1</sup> Walasinee Sakcamduang<sup>1\*</sup>

## *Abstract*

A 1 year and 4 months old, intact female French Bulldog was presented because of weakness, anorexia, and vomiting for 3 days. Laboratory findings included azotemia, hyponatremia, hypochloremia, sodium to potassium (Na:K) ratio was 23.88, and the lower level of basal cortisol concentration than the detection limit. The small size of both adrenal glands obtained from abdominal ultrasonography. Subsequently, the adrenocorticotrophic hormone (ACTH) stimulation test was performed, and the diagnosis of hypoadrenocorticism was confirmed. The desoxycorticosterone pivalate (DOCP) with a smaller dose and lesser frequency than the recommendation of 2.2 mg/kg every 25 days. The dog received DOCP subcutaneous injection at a dose of 1.5 mg/kg initially and followed by 1.37 mg/kg 55 days after the first injection, 1.37 mg/kg 28 days after the second injection, and more than 84 days after a dose of 1.37 mg/kg of the third injection. Glucocorticoid administrations were in recommended doses for the whole period of management. Improvement of clinical manifestations and laboratory parameters of the dog was observed a week later after the DOCP intervention. A smaller than recommended dose and lesser frequency of the DOCP with prednisolone seems adequate for controlling clinical problems in the successful management of the hypoadrenocorticism in a French Bulldog.

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**Keywords:** Addison's disease, cortisol, desoxycorticosterone pivalate, dog, hypoadrenocorticism

<sup>1</sup>Faculty of Veterinary Science, Mahidol University, Phutthamonthon 4 Road, Salaya, Phutthamonthon, Nakhon Pathom, 73170 Thailand

\*Correspondence: [walasinee.sak@mahidol.edu](mailto:walasinee.sak@mahidol.edu) (W. Sakcamduang)

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## Introduction

Hypoadrenocorticism (Addison's disease) is commonly mistaken for other conditions from the vague and nonspecific clinical signs attributable to its multiple systems involvement. This can lead to time-consuming, financial and emotional stress. A successful diagnosis solves a medical mystery, saves a sick animal and addresses a promising prognosis. Spontaneous recovery has not been reported (Scott-Moncrieff, 2015).

The prevalence in dogs has been approximated at 0.3% to 1.1%, of which the typical age is between 2 and 6 years (Bellumori *et al.*, 2013). As in humans, females (bitches) represent a higher proportion than male dogs. The predisposed breeds are the Portuguese Waterdog, the Standard Poodle, the Nova Scotia Duck Tolling Retriever and the Bearded Collie, which have inherited an autosomal recessive trait (Scott-Moncrieff, 2015).

Hypoadrenocorticism has a variety of clinical manifestations and diagnostic findings that imitate other diseases. The typical electrolyte changes of hyperkalemia and hyponatremia with a low sodium and potassium ratio combined with a low lymphocyte count have led to suspicions of the illness. An adrenocorticotropic hormone (ACTH) stimulation test is required for a definitive diagnosis (Seth *et al.*, 2011).

Treatment of hypoadrenocorticism consists of glucocorticoid, prednisolone and mineralocorticoid; and either desoxycorticosterone pivalate (DOCP) or fludrocortisone supplementation. The difference in DOCP that it is a long-acting mineralocorticoid without the composition of glucocorticoid, instead of fludrocortisone containing both supplementations (Scott-Moncrieff, 2015).

This case study was reported because the dog presented with no improvement palliative treatment by a local veterinary practice as the dog had non-specific clinical manifestations and was a non-

predisposing breed. The logical approach was conducted for a definitive diagnosis. Monitoring clinical signs and electrolytes guided dose and frequency of medical treatment.

## Materials and Methods

**Signalment & History:** A 1 year 4 months old, intact female French Bulldog was presented at Prasu-Arthorn Animal Hospital, Mahidol University, Thailand, because of exhibiting weakness, anorexia and vomiting for three days. It had previously been prescribed marbofloxacin, sucralfate and fluid therapy from a local clinic for three days without improvement. The dog was up to date in vaccination, heartworm prophylaxis and tick prevention.

**Physical examination:** The dog was depressed. Its rectal temperature was normal at 101.4 °F; the heart rate was 128 beats per minute with a normal heart sound; the respiratory rate was 28 breaths per minute with a normal lung sound, pink mucous membranes and a capillary refill time (CRT) of less than 2 seconds. Its body weight was 13.9 kg and the body condition score was 5/9. The dog did not show any abnormality from abdominal palpation. The systolic blood pressure was 160 mmHg.

**Diagnostic plan, initial treatment plan and outcome:** The dog was admitted for diagnosis, treatment and monitoring. Blood was collected for a complete blood count (CBC), serum biochemistry and electrolyte profiles. Urine was also collected by cystocentesis for urinalysis. Abnormalities included polycythemia, azotemia, hyperproteinemia, hyponatremia, hypochloremia and the Na:K ratio was 23.9:1 (Table 1). Urinalysis showed urine specific gravity at 1.030, pH 6.0 and no other abnormalities were detected.

**Table 1** Hematology, serum biochemistry, and serum electrolyte values measured before admission (day 0).

Parameters	Values	References	Parameters	Values	References
Red blood cell	8.65	5.0-9.0 × 10 <sup>6</sup> /μL	Alkaline phosphatase	30	23-212 U/L
Hemoglobin	20.6	10-18 g/dL	Alanine aminotransferase	41	10-100 U/L
Hematocrit	61	35-55%	Blood urea nitrogen (BUN)	59	7-27 mg/dL
MCV	70.5	60-77 fL	Creatinine	2.55	0.5-1.8 mg/dL
MCH	23.8	20-25 pg	Albumin	3.7	2.7-3.8 g/dL
MCHC	33.8	32-36 g/dL	Total protein	7.2	5.2-8.2 g/dL
Platelets	236	200-500 × 10 <sup>3</sup> /μL	Potassium (K)	5.34	3.5-5.8 mmol/L
Plasma protein	9	6.0-7.5	Sodium (Na)	127.5	142-152 mmol/L
RDW	13	12-15%	Chloride (Cl)	94.6	109-122 mmol/L
White blood cell count	11.65	6.0-17.0 × 10 <sup>3</sup> /μL	Carbondioxide (CO <sub>2</sub> )	17	18-29 mmol/L
Monocyte	0.93	0.2-1.7 × 10 <sup>3</sup> /μL	Sodium to potassium ratio	23.88	27.1 - 40:1
Neutrophil	8.5	3.6-13.1 × 10 <sup>3</sup> /μL	Canine pancreatic lipase	< 50	0-199 ng/mL
Lymphocyte	2.1	0.7-5.1 × 10 <sup>3</sup> /μL			
Eosinophil	0.12	0.1-1.7 × 10 <sup>3</sup> /μL			

MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red blood cell distribution width.

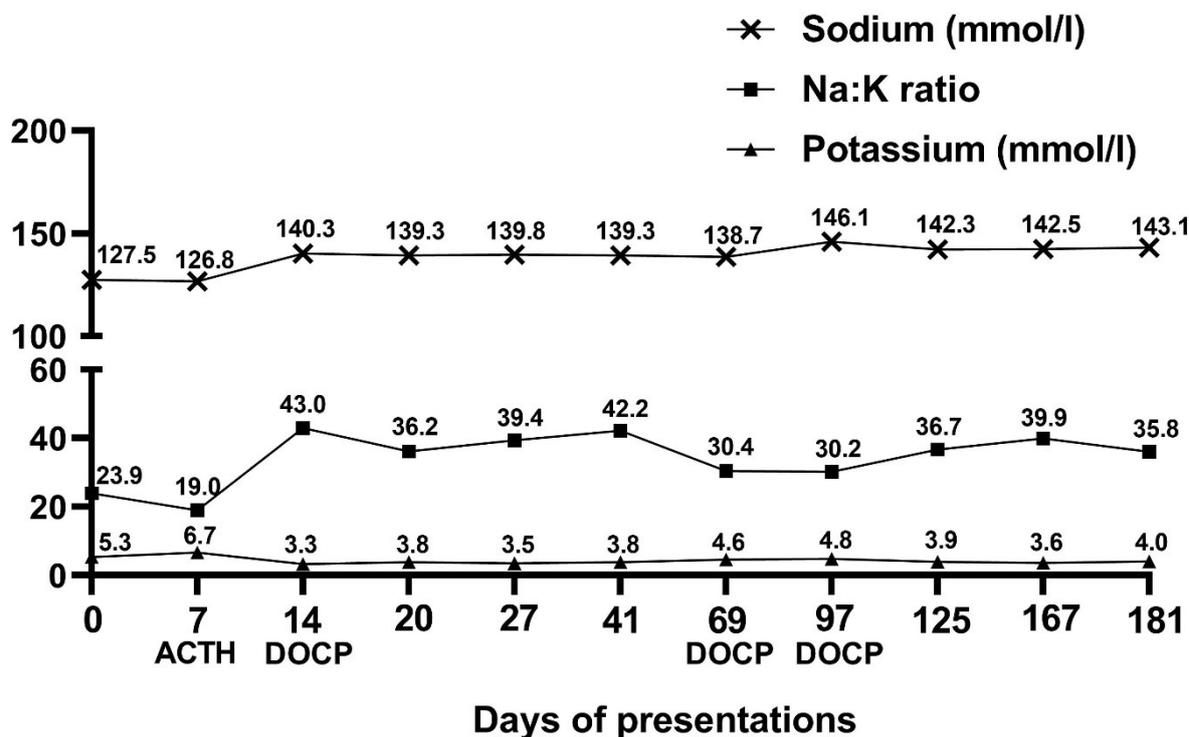
References obtained from the Laboratory unit, Prasu-arthorn Animal Hospital, Faculty of Veterinary Science, Mahidol University.

The dog was catheterized intravenously (IV) for normal saline (0.9% NSS) infusion at 4.61 ml/kg/h for the first 24 hours, omeprazole (0.5 mg/kg IV q 12 h) and ondansetron (0.5 mg/kg IV q 24 h). Urine output was also monitored and yielded 1.8 ml/kg/h for the first 4 hours.

In the first 24 hours, the dog improved with no clinical abnormalities. The azotemia was resolved but there was no improvement in the hyponatremia or hypochloremia. The Na:K ratio was 23.4:1. It was measured for basal cortisol concentration and <0.23 µg% was found, less than the normal reference range. Abdominal ultrasonography was performed and showed no abdominal organ abnormalities, except for a smaller size of both adrenal glands. The dog was discharged on day 3.

It underwent an ACTH stimulation test 4 days later (day 7) and cortisol levels <0.23 µg% before and one hour after the intravenous injection of 63 µg (dose 5 µg/kg) of compounded tetracosactide acetate (Synacthen®) were found. Pre- and post-ACTH cortisol concentrations less than the reference range for basal cortisol (2 µg%) confirmed the diagnosis of hypoadrenocorticism (Scott-Moncrieff, 2015).

**Long term management, monitoring and outcome:** The dog was injected with desoxycorticosterone pivalate (DOCP, Zycortal, Dechra) 1.5 mg/kg SC on day 14 after the first visit. It was discharged with only prednisolone 0.5 mg/kg PO q 12 h. It re-visited 7 days later without vomiting or diarrhea. It was given tapered prednisolone to 0.76 mg/kg PO q 24 h on day 19 and was scheduled to revisit every 2 weeks for monitoring following the DOCP intervention. Serum Na:K ratio and potassium concentration were the major information for the next DOCP intervention. If the Na:K ratio were less than 30 and potassium concentration were in the normal range, the DOCP injection would have worked. After monitoring the results, the dog was injected DOCP at a dose of 1.37 mg/kg on day 69, and day 97, whereas the dosage of prednisolone had been 0.57 mg/kg PO q 24 on day 26, 0.38 mg/kg q 24 h on day 69 and 0.18 mg/kg PO q 24 h since day 111 to the last examination on day 181. Prednisolone had been maintained at a dose of 0.18 mg/kg q 24 h after day 181. We followed up the clinical signs and measured serum sodium, potassium and Na:K ratio, lastly on day 181 (20<sup>th</sup> August 2020), and no more DOCP was administered after day 97 (Figure 1).



**Figure 1** Sodium and potassium concentration (mmol/L) measured in the serum of the dog for 181 days. Day 0, the first visit; day 7, ACTH stimulation test; day 14, 67, and 97 administered desoxycorticosterone pivalate (DOCP).

**Results and Discussion**

Desoxycorticosterone pivalate (DOCP) and prednisolone were chosen for treating the clinical abnormalities. We did not choose fludrocortisone for sole prescription as DOCP is more convenient for adjusting mineralocorticoid dosage than fludrocortisone and even fludrocortisone contains both

mineralocorticoid and glucocorticoid. The appropriate dose of DOCP for treating this case was 1.5 mg/kg subcutaneous injection every 28-30 days and the injectable period could be adjusted followed by serum potassium concentration (Sieber-Ruckstuhl *et al.*, 2019). Prednisolone 0.5 mg/kg PO q 12 h was prescribed as a glucocorticoid supplement in the first week after we discharged the dog and planned to taper the dose

dependent upon clinical signs. After the first administration of DOCP, we found only mild hyponatremia for several weeks but the Na:K ratios were between 36.2:1 to 43.0:1. These were from low potassium levels suggested to be from DOCP administration (Baumstark *et al.*, 2014). We monitored the dog every 4 weeks and found sodium, potassium and Na:K ratios within normal limits after the last administration of DOCP on day 91. Therefore, no DOCP was administered on day 181, the last day of examination. The dog had been well with only prednisolone orally at a dose of 0.19 mg/kg q 24 h. A lower initial dose had made no difference in survival or post-treatment serum sodium, potassium or Na:K ratio compared to the recommended dose at 2.2 mg/kg (Bates *et al.*, 2013). Importantly, client education on the perfect dose can change for any reason. We recommended monitoring every 4 weeks.

Major abnormalities of the hypoadrenocorticism dogs include hyponatremia, hyperkalemia, non-regenerative anemia and lymphocytosis (Scott-Moncrieff, 2015). Nevertheless, these changes are not present in all cases. Fewer clinical presentations can be a significant diagnostic consideration. Complete blood count, serum biochemistry and urinalysis are routine diagnostic techniques. This dog was, however, presented without any indication of hypoadrenocorticism. We performed routine diagnostic techniques without measuring the electrolytes at first. When we found azotemia with non-specific gastrointestinal signs and hemoconcentration, we could have missed the clues that this dog had hypoadrenocorticism if we had decided not to evaluate serum electrolytes. Indeed, electrolytes are essential diagnostic tools to expose additional problems. Azotemia was resolved 24 hours after fluid therapy. It was likely pre-renal azotemia consequent upon hemoconcentration.

This was a rare case that found hypoadrenocorticism in a French bulldog since the predisposed breeds for the disease are mentioned above. The prognosis for dogs with naturally occurring hypoadrenocorticism is excellent. The average survival time for treated dogs is 4.7 years and most of them die from other health problems (Lathan and Thompson, 2018).

In conclusion, we suggest a serum electrolyte technique should be preferred as one of the screening tests in azotemia case with an unclear history since the Na:K ratio is meaningful information for a diagnosis of hypoadrenocorticism. The ACTH stimulation test is a definitive diagnosis for suspected cases. A smaller than recommended dose and lesser frequency of the DOCP with prednisolone seemed adequate for controlling clinical problems in the successful management of the hypoadrenocorticism in a French Bulldog.

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University, Salaya, Phutthamonthon, Nakhon Pathom, 73170 Thailand.

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