

Effect of glucocorticoid administration on serum aldosterone concentration in clinically normal dogs

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Objective—To evaluate the effects of oral administration of anti-inflammatory dosages of prednisone for 28 days on serum aldosterone, cortisol, and electrolyte concentrations in clinically normal dogs.

Animals—10 dogs.

Procedures—On days 1 through 28, 5 dogs received prednisone (0.55 mg/kg, PO, q 12 h) and 5 dogs received similar treatments with a placebo (empty capsules). Serum cortisol and aldosterone concentrations before and after ACTH stimulation testing and serum electrolyte concentrations were measured before (day 0 [baseline]), during (days 7, 14, 21, and 28), and after (days 35 and 42) treatment.

Results—At baseline, variables did not differ between the 2 groups. Serum cortisol concentrations before and after ACTH stimulation testing did not change from baseline values in placebo-treated dogs. In prednisone-treated dogs, serum chloride and corrected chloride concentrations were significantly lower on days 7, 14, 21, and 28 and serum bicarbonate concentrations were significantly higher on days 14, 21, and 28, compared with baseline values. Serum cortisol concentrations before and after ACTH stimulation testing were significantly lower than baseline values during prednisone treatment. Serum aldosterone concentration after ACTH stimulation testing was significantly lower than baseline on day 35 (ie, 1 week after discontinuation of prednisone treatment) but returned to baseline by day 42 in prednisone-treated dogs.

Conclusions and Clinical Relevance—Administration of anti-inflammatory dosages of prednisone caused significant changes in serum chloride, bicarbonate, and cortisol concentrations in clinically normal dogs. Although ACTH-stimulated serum aldosterone concentrations were unchanged from baseline during glucocorticoid administration, values decreased after treatment cessation but quickly returned to baseline values. (*Am J Vet Res* 2010;71:649–654)

Glucocorticoids suppress ACTH synthesis and secretion by the adenohypophysis. Extended exogenous glucocorticoid administration causes atrophy of the adrenocortical zona fasciculata and reticularis. Weaning patients off glucocorticoid treatment in a stepwise fashion is recommended to allow recovery from adrenocortical suppression and restoration of appropriate responses to stressful situations.¹ Although the effects of exogenous glucocorticoid treatment, regardless of route of administration, on cortisol secretion are known,^{2–5} similar evaluation of feedback effects of such

treatment on circulating aldosterone concentration has not been performed, to our knowledge.

Adrenocorticotrophic hormone has a role in the control of aldosterone synthesis and release from the zona glomerulosa of the adrenal gland. Daily ACTH administration to rats linearly increases the volume of the zona glomerulosa as a function of the number of days of treatment, and conversely, daily dexamethasone administration linearly decreases the volume.⁶ At a functional level, ACTH deficiency causes decreases in serum aldosterone concentration. In a study⁷ in dogs, the serum aldosterone concentration and concentrations of other adrenal steroid hormones were significantly decreased at 6 to 10 hours after hypophysectomy, compared with findings in dogs that underwent sham hypophysectomy. In that study,⁷ serum aldosterone and corticosterone concentrations decreased to 42% and 12% of prehypophysectomy values, respectively.

Thus, ACTH deficiency secondary to glucocorticoid administration could suppress serum aldosterone concentration, but to our knowledge, this has not been widely studied in dogs. In 2 studies,^{8,9} the acute effects of dexamethasone administration (0.1 mg/kg, IV) on

Received January 28, 2009.

Accepted June 1, 2009.

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Presented in part at the 28th Annual Veterinary Internal Medicine Forum, San Antonio, Tex, June 2008.

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serum aldosterone concentration in healthy dogs were evaluated; significant suppression of serum aldosterone concentration from pretreatment values was not evident at 2 hours after the dexamethasone injection but was evident at the 3- and 4-hour time points.⁸ A single study¹⁰ of chronic effects of glucocorticoid administration on plasma aldosterone concentration revealed significant suppression of basal aldosterone concentrations in dogs with iatrogenic hyperadrenocorticism. The extent to which glucocorticoid administration can suppress aldosterone secretion over time or the dose of glucocorticoid or duration of treatment required to cause that suppression is unknown.

Glucocorticoids are used to treat a wide variety of diseases. If treatment is discontinued abruptly, clinical signs of adrenocortical insufficiency can develop. Appropriate treatment for clinical signs of hormone deficiency that develop after rapid glucocorticoid withdrawal is believed to consist solely of glucocorticoid administration. However, such treatment may not adequately address problems such as hypotension that can be induced by aldosterone deficiency. In addition, patients are evaluated at times for spontaneous hypoadrenocorticism after discontinuation of glucocorticoid treatment via assessment of circulating electrolyte and cortisol concentrations. A supposition has been that if serum aldosterone concentration was affected, hypocortisolism was more likely a result of naturally occurring disease than an iatrogenic cause because glucocorticoid administration was assumed to not affect serum aldosterone concentration. This assumption, however, may not be valid.

The ACTH stimulation test evaluates adrenal gland function and is typically used clinically to assess glucocorticoid reserve. However, the test can also be used to evaluate aldosterone secretory capacity,⁹⁻¹² and test results accurately reflect disease status in hypofunctional states. Serum aldosterone concentration is low in dogs with primary hypoadrenocorticism when hyponatremia and hyperkalemia are present.¹¹ Furthermore, in some patients with electrolyte concentrations within the reference range despite ACTH stimulation results indicative of cortisol deficiency, serum aldosterone concentrations before and after ACTH stimulation were less than the lower reference limit. In those dogs, the disease state progressed to complete aldosterone deficiency, ultimately necessitating administration of mineralocorticoid supplements.¹¹ Thus, measurement of serum aldosterone concentration after ACTH stimulation can reveal insufficiencies in mineralocorticoid secretion that are not detected by measurement of basal concentrations alone.

Therefore, the purpose of the study reported here was to evaluate the effects of oral administration of anti-inflammatory dosages of prednisone for 28 days on serum concentrations of aldosterone and cortisol (both before and after ACTH stimulation), sodium, chloride, potassium, and bicarbonate; anion gap; and osmolality in clinically normal dogs. Our hypothesis was that exogenous glucocorticoid administration would significantly decrease basal and ACTH-stimulated serum aldosterone concentrations and that hyponatremia, hypochloremia, or hyperkalemia (or combinations thereof) would develop.

Materials and Methods

Animals—Ten sexually intact American Foxhounds (4 males and 6 females [1 in estrus]) were used in the study. The dogs were 1 to 5 years old and weighed 18 to 27 kg. Dogs were each considered to be clinically normal on the basis of physical examination findings and results of a CBC, serum biochemical analysis, urinalysis, and heartworm occult antigen testing. Those assessments were performed on the day before experimental treatments were commenced (day 0). On day 0, anion gap, serum osmolality, and serum cortisol and aldosterone concentrations before and after ACTH stimulation were also assessed in each dog. All dogs were housed in standard university kennels, were fed dry adult maintenance food, and had access to water ad libitum. The Auburn University Institutional Animal Care and Use Committee approved the study.

Experimental protocol—The dogs were randomly assigned to receive treatment with prednisone (0.55 mg/kg, PO, q 12 h) or treatment with placebo on a similar schedule (5 dogs/group). The investigators were blinded to the treatment assignment. Prednisone was administered in the form of tablets^a that were placed into opaque gelatin capsules by a pharmacist; the placebo consisted of empty capsules. The medications were administered at 8 AM and 8 PM daily for 28 days (days 1 to 28) and then discontinued for the remaining 14 study days (days 29 to 42).

Physical examination findings; serum concentrations of sodium, chloride, potassium, and bicarbonate; anion gap; serum osmolality; and serum cortisol and aldosterone concentrations before and after ACTH stimulation obtained on day 0 were used as pretreatment baseline data. These assessments were repeated weekly for each dog until the end of the study (ie, on days 7, 14, 21, 28, 35, and 42).

Sample collections and assay procedures—At each time point, a blood sample (approx 5 mL) was collected via jugular venipuncture from each dog. The sample was placed into an evacuated glass tube containing EDTA and an evacuated glass tube containing lithium heparin for a CBC determination and assessments of serum electrolyte concentrations, anion gap, and serum osmolality, respectively. A urine sample was obtained via ultrasound-guided cystocentesis or free catch. All clinicopathologic analyses and urinalyses were performed on the day of sample collection.

For the ACTH stimulation tests, a prestimulation blood sample (2 mL) was obtained via jugular venipuncture from each dog, and cosyntropin^b (1.0 µg/kg, IV) was administered into a cephalic vein. At 20^c and 60¹³ minutes after ACTH stimulation, a blood sample (2 mL) was collected via jugular venipuncture for measurement of serum aldosterone and cortisol concentrations, respectively. Samples collected for determination of hormone concentrations were placed in anticoagulant-free glass tubes, allowed to clot for at least 30 minutes, and centrifuged for 5 minutes; the serum was separated and frozen at -20°C until the assays were performed in a single batch. Serum samples used for assessment of aldosterone^d and cortisol^e concentrations

were assayed in duplicate by use of a previously validated radioimmunoassay for each hormone.^{14,15} Sensitivities of the assays were 14 nmol/L and 14 pmol/L for cortisol and aldosterone concentrations, respectively. For statistical purposes, values less than the lower limit of quantitation of the assay were recorded as 7 nmol/L and 7 pmol/L for serum cortisol and aldosterone concentrations, respectively. According to the manufacturer, the cross-reactivity for prednisone in the aldosterone assay is < 0.07%. In addition, the dogs had not received prednisone during the 12-hour period before measurement of serum cortisol concentration, and the test was performed immediately prior to the morning prednisone administration, which was likely to be adequate to prevent the accumulation of a sufficient amount of prednisone in the serum to affect apparent serum cortisol concentration.¹⁶ For purposes of the study, the corrected serum chloride concentration was calculated by use of a formula¹⁷ as follows:

$$\text{Serum chloride concentration (corrected)} = \text{Cl}^- \text{ concentration (measured)} \times (\text{Na}^+ \text{ concentration [low reference limit]} / \text{Na}^+ \text{ concentration [measured]})$$

Statistical analysis—Analysis was performed by use of a commercial program.^f For each variable, comparisons were made between groups on day 0 by use of a Mann-Whitney *U* test. In addition, comparisons of data obtained at the various time points were made against baseline values within a group by use of a repeated-measures ANOVA on ranks. If a significant difference was found, post hoc comparisons were made by use of the Student-Neuman-Keuls method. Significance was set at a value of $P \leq 0.05$.

Results

Five dogs were each randomly assigned to receive treatment with prednisone or placebo. The prednisone-treated group included 3 males and 2 females (mean \pm SD weight, 23.0 \pm 2.2 kg). One of the female dogs in this group was in estrus. The placebo-treated group included 1 male and 4 females (mean weight, 23.9 \pm 2.0 kg).

On day 0, no significant difference was detected between prednisone- and placebo-treated dogs with respect to any assessed variable. In the prednisone-treated group, differences in basal and ACTH-stimulated serum cortisol concentrations were detected over time; serum cortisol concentrations before and after ACTH stimulation were significantly lower than baseline values on days 7, 14, 21, and 28 were no longer significantly different from baseline and all basal and some ACTH-stimulated cortisol concentrations were within the reference range (basal cortisol concentration reference range, 10 to 160 nmol/L; ACTH-stimulated cortisol concentration reference range, 220 to 560 nmol/L) on days 35 and 42 (Figure 1; Table 1). No change in basal or ACTH-stimulated serum cortisol concentration was evident in dogs receiving the placebo treatment. In the prednisone-treated group, the ACTH-stimulated serum aldosterone concentration was significantly lower than baseline on day 35 (the first week after cessation of prednisone administration), but returned to baseline concentration by day 42. No significant changes were

detected in basal aldosterone concentration in either group or in ACTH-stimulated serum aldosterone concentration in dogs receiving placebo.

Interestingly, despite a lack of a significant change in serum aldosterone concentration during treatment, other serum biochemical variables changed significantly. Serum chloride concentration was significantly lower than baseline value in the prednisone-treated dogs during the treatment period (ie, days 7, 14, 21, and 28), but returned to baseline values after discontinuation of prednisone administration (Table 2). To evaluate changes in water balance in relation to changes in serum sodium concentration, corrected serum chloride concentration was calculated¹⁷; significant differences from baseline for that variable were the same as those identified for measured serum chloride concentration (Figure 2). In the prednisone-treated dogs, serum bicarbonate concentrations were significantly higher than baseline on days 14, 21, and 28 (Figure 3). Anion gap was significantly higher than baseline value in the prednisone-treated dogs on days 7, 14, and 28. No significant changes in serum potassium concentration were detected in either group throughout the study. Data regarding serum sodium concentration and os-

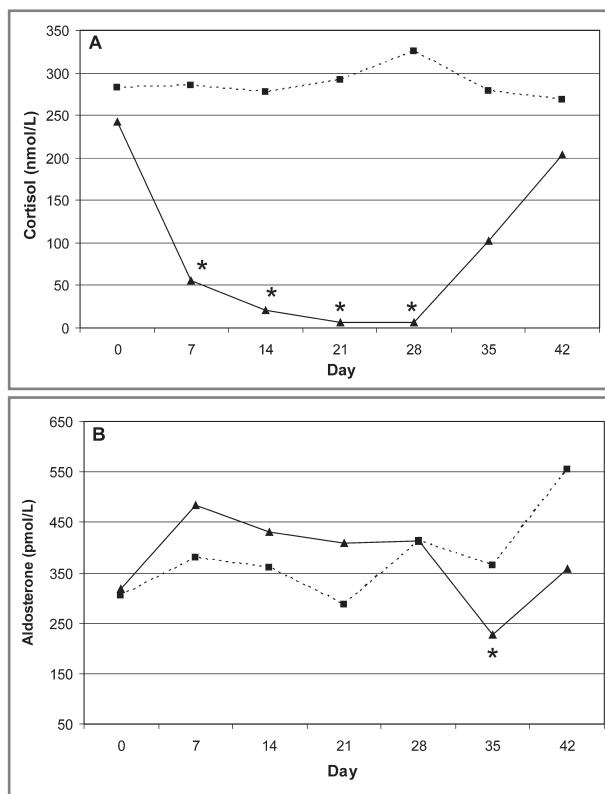


Figure 1—Median serum cortisol (A) and serum aldosterone (B) concentrations at 60 and 20 minutes, respectively, after ACTH stimulation testing (administration of 1.0 μ g of cosyntropin/kg, IV) in 5 clinically normal dogs that were treated with prednisone (0.55 mg/kg, PO, q 12 h [black triangles]) and 5 clinically normal dogs that were treated with placebo (1 empty capsule, PO, q 12 h [black squares]) for 28 days (beginning day 1). Assessments were performed before (day 0 [baseline]), during (days 7, 14, 21, and 28), and after (days 35 and 42) treatment. Reference range for serum cortisol concentration in dogs is 220 to 560 nmol/L; there is no established reference range for serum aldosterone concentration. *Within a group, value at this time point is significantly ($P \leq 0.05$) different from the baseline value.

Table 1—Median (range) serum aldosterone and cortisol concentrations before and after ACTH stimulation testing (basal and ACTH-stimulated concentrations, respectively) in 5 clinically normal dogs that were treated with prednisone (0.55 mg/kg, PO, q 12 h) and 5 clinically normal dogs that were treated with placebo (1 empty capsule, PO, q 12 h) for 28 days (beginning day 1).

Day	Aldosterone (pmol/L)				Cortisol (nmol/L)			
	Prednisone-treated dogs		Placebo-treated dogs		Prednisone-treated dogs		Placebo-treated dogs	
	Basal concentration	ACTH-stimulated concentration	Basal concentration	ACTH-stimulated concentration	Basal concentration	ACTH-stimulated concentration	Basal concentration	ACTH-stimulated concentration
0	7 (7–236)	319 (233–699)	7 (7–272)	305 (214–683)	38 (20–148)	242 (140–467)	68 (21–247)	283 (189–352)
7	78 (7–158)	483 (422–588)	7 (7–500)	380 (283–1,110)	7* (7–7)	56* (22–75)	75 (43–274)	285 (203–383)
14	81 (7–236)	430 (297–605)	7 (7–83)	361 (266–774)	7* (7–7)	21* (7–41)	70 (18–180)	277 (207–358)
21	7 (7–69)	408 (344–533)	7 (7–164)	286 (258–699)	7* (7–7)	7* (7–22)	99 (23–194)	292 (245–355)
28	105 (7–136)	414 (358–516)	7 (7–67)	414 (244–588)	7* (7–7)	7* (7–7)	94 (24–245)	326 (235–403)
35	7 (7–19)	228* (100–352)	81 (7–183)	364 (219–643)	29 (19–86)	102 (86–309)	109 (46–271)	279 (180–370)
42	7 (7–67)	358 (125–647)	7 (7–161)	555 (136–566)	51 (19–93)	203 (181–401)	53 (30–222)	268 (131–283)

Assessments were performed before (day 0 [baseline]), during (days 7, 14, 21, and 28), and after (days 35 and 42) treatment. The ACTH-stimulated serum aldosterone and serum cortisol concentrations were determined at 20 and 60 min after administration of cosyntropin (1.0 µg/kg IV), respectively. Reference ranges for basal and ACTH-stimulated serum cortisol concentrations in dogs are 10 to 160 nmol/L and 220 to 560 nmol/L, respectively; there are no established reference ranges for basal and ACTH-stimulated serum aldosterone concentrations.
*Within a variable in a group, median value at this time point was significantly ($P \leq 0.05$) different from the baseline value.

Table 2—Median (range) serum potassium, sodium, and chloride concentrations; serum osmolality; and anion gap in 5 clinically normal dogs that were treated with prednisone (0.55 mg/kg, PO, q 12 h) and 5 clinically normal dogs that were treated with placebo (1 empty capsule, PO, q 12 h) for 28 days (beginning day 1).

Day	Potassium (mEq/L)		Sodium (mEq/L)		Chloride (mEq/L)		Osmolality (mOsm/L)		Anion gap (mEq/L)	
	Prednisone-treated dogs	Placebo-treated dogs	Prednisone-treated dogs	Placebo-treated dogs	Prednisone-treated dogs	Placebo-treated dogs	Prednisone-treated dogs	Placebo-treated dogs	Prednisone-treated dogs	Placebo-treated dogs
0	4.0 (3.6–4.4)	3.5 (3.2–4.1)	149 (147–153)	149 (148–152)	112 (110–114)	111 (109–112)	305 (302–313)	306 (302–310)	25.3 (24–28)	25.7 (24–28)
7	3.6 (3.4–3.9)	3.5 (3.1–3.9)	145* (142–148)	147* (144–149)	101* (100–102)	110 (106–111)	297* (291–303)	301* (296–304)	29.7* (27–34)	25.8 (24–27)
14	3.7 (3.4–4.1)	3.8 (3.0–3.8)	146* (146–151)	148* (145–151)	101* (100–105)	110 (104–114)	300* (300–309)	304* (298–308)	28.9* (26–32)	24.8 (22–27)
21	3.8 (3.0–3.8)	3.6 (3.1–3.9)	144* (142–149)	147* (144–149)	101* (99–103)	110 (107–111)	296* (292–304)	300* (295–305)	28.1 (25–31)	23.7 (23–25)
28	3.6 (3.5–3.8)	3.7 (3.3–4.1)	146* (144–148)	147* (145–149)	99* (97–102)	110 (105–110)	300* (295–303)	301* (297–305)	29.1* (25–32)	24.8 (24–25)
35	3.6 (3.2–3.9)	3.7 (3.3–4.2)	149 (149–151)	149 (146–149)	110 (108–112)	111 (109–112)	306 (304–309)	305 (299–305)	25.3 (23–30)	24.3 (21–27)
42	3.5 (3.3–3.7)	3.8 (3.1–3.9)	147* (144–148)	147* (144–148)	108 (107–110)	108 (106–112)	301* (295–303)	300* (295–304)	25.4 (20–27)	25.4 (23–27)

Reference ranges for these variables in dogs are as follows: serum potassium concentration, 3.5 to 5.9 mEq/L; serum sodium concentration, 146 to 160 mEq/L; serum chloride concentration, 108 to 125 mEq/L; osmolality, 295 to 317 mOsm/kg; and anion gap, 11.8 to 23.1 mEq/L.
See Table 1 for key.

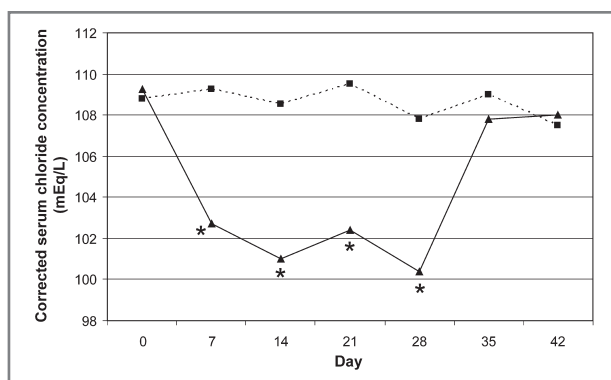


Figure 2—Median corrected serum chloride concentrations in clinically normal dogs that were treated orally with prednisone (0.55 mg/kg) or placebo every 12 hours for 28 days (5 dogs/group). Reference range for corrected serum chloride concentration in dogs is 108 to 125 mEq/L. See Figure 1 for key.

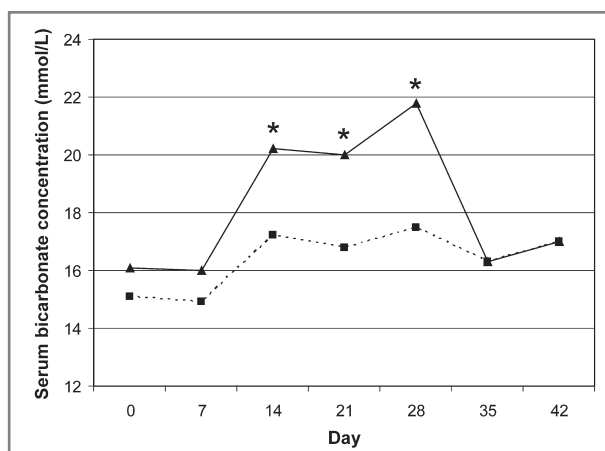


Figure 3—Median serum bicarbonate concentrations in clinically normal dogs that were treated orally with prednisone (0.55 mg/kg) or placebo every 12 hours for 28 days (5 dogs/group). Reference range for serum bicarbonate concentration in dogs is 13.9 to 30 mmol/L. See Figure 1 for key.

molality were confounded as these variables decreased significantly over time in the placebo-treated group and were therefore not analyzed further.

Discussion

Disease states associated with decreased adrenal

function can cause a variety of clinical signs depending upon the adrenocortical layers and hormones affected. Mineralocorticoid deficiency causes hyperkalemia as well as sodium and water losses that result in hypovole-

mia. The clinical signs of glucocorticoid deficiency are subtle and include poor appetite, lethargy, and gastrointestinal tract problems. Glucocorticoids are commonly prescribed in veterinary medicine and their negative feedback effects on ACTH secretion (thereby causing cortisol deficiency) are well established. Given the role of ACTH in aldosterone secretion, administration of exogenous glucocorticoids could result in hypoaldosteronemia. Because mineralocorticoid deficiency could potentially be life threatening, knowledge of whether glucocorticoid administration could cause hypoaldosteronemia would be crucial in determining how to effectively treat patients that develop adverse effects associated with abrupt discontinuation of exogenous glucocorticoid treatment.

A dose of 1.0 µg of cosyntropin/kg was chosen for ACTH stimulation testing in the present study. In healthy dogs, doses of both 1.0 and 5.0 µg/kg maximally stimulate cortisol secretion with peak plasma cortisol concentrations detected at 60 minutes after injection.¹³ Although the 5 µg/kg dose is used conventionally, administration of 1.0 µg/kg is a more sensitive means of detecting subtle glucocorticoid insufficiency.¹⁴ The maximally stimulating dose of cosyntropin and time of peak response with respect to aldosterone are unknown. However, after administration of 1.0 µg of cosyntropin/kg, the interval to maximal aldosterone response is 20 minutes.^c

Measurement of serum cortisol concentration revealed the expected suppression of cortisol release in the prednisone-treated dogs during drug administration with no change in the placebo-treated group. In comparison, serum aldosterone concentration in the prednisone-treated dogs decreased significantly from baseline only on day 35, that is, 7 days after discontinuation of treatment. The reason for the delayed change is not clear. The main stimuli of aldosterone secretion are angiotensin II and hyperkalemia.¹⁸ Although endogenous plasma ACTH concentrations were not measured in the present study, given the increase in serum cortisol concentrations from day 28 to day 35, endogenous ACTH concentrations of serum cortisol concentrations to within the reference range by day 35, endogenous ACTH concentrations would be expected to be within or greater than the reference range at that time. Hypokalemia was not evident in the prednisone-treated dogs on day 35. However, a single blood sample was collected from each dog once a week for measurement of serum potassium concentration, and hypokalemia may have been present on days 29 to 34. The potential role of alterations in angiotensin II concentrations in causing the suppressed serum aldosterone concentrations was not evaluated in our study.

One of the dogs included in the prednisone-treated group was a sexually intact female dog that was in estrus on day 0. However, inclusion of this dog was unlikely to have an effect on the results. It is known that estradiol has no effect on fluid secretion or chloride transport in Madin-Darby canine kidney cells¹⁹ and estradiol causes sodium retention in dogs^{20,21} (the opposite of findings of the present study). Progesterone appears to have no effect on sodium or potassium excretion in clinically normal dogs.²⁰ Also, we repeated the statistical analyses

after removing data obtained from the dog in question, and the results did not change (data not shown).

The effect of glucocorticoid administration on serum electrolyte concentrations has not been widely studied, to our knowledge. In the present study, marked and significant decreases (from baseline values) in measured and corrected serum chloride concentrations were evident on days 7, 14, 21, and 28 in the prednisone-treated dogs. However, the serum bicarbonate concentrations were not as high and the serum sodium concentrations not as low as expected for the degree of hypochloremia. Similar changes were detected in healthy dogs subsequent to administration of triamcinolone at a dose of 0.5 mg/kg (IM, q 12 h for 6 to 9 days²²) or prednisone at a dose of 2.2 mg/kg (PO, q 12 h for 42 days²³). However, changes in serum electrolyte concentrations in dogs were not detected during and 2, 4, and 7 weeks after oral administration of 0.55 mg of prednisone/kg every 12 hours for 35 days²⁴ or after topical ocular administration of 1% prednisone acetate ophthalmic suspension in which 4 mg of prednisone/d (mean dosage, 0.75 mg/kg/d) was provided for 2 weeks followed by 2.67 mg of prednisone/d (mean dosage, 0.5 mg/kg/d) for 2 weeks.⁴ In the latter study,⁴ blood samples were collected at the end of the second and fourth weeks of glucocorticoid administration and 2 weeks after discontinuing treatment. The reason for the difference in findings between both aforementioned studies and the present one is not clear. Suppression of cortisol concentration subsequent to ocular administration of the ophthalmic preparation was attributed to the effect of the prednisone following systemic absorption. Given that the evaluation of corrected serum chloride concentration did not change results of the present study, a direct effect of oral glucocorticoid administration on serum chloride concentration is possible. Alternatively, because serum bicarbonate concentration was not increased to the expected extent, a nonmeasured anion may have been present.²² The anion gap was significantly increased from baseline on days 7, 14, and 28, which was most likely a result of a decrease in serum chloride concentration.

One limitation of our study was the duration of treatment. A previous study¹⁰ found significantly suppressed basal and ACTH-stimulated plasma aldosterone concentrations in dogs with iatrogenic hyperadrenocorticism, compared with findings in healthy dogs. The difference between our study findings and those of the previous study¹⁰ may be attributable to the dosage or duration of glucocorticoid administration or both. In another investigation²⁴ involving healthy dogs that were treated for 5 weeks with the same dosage of prednisone as that used in the present study, the only systemic sign of glucocorticoid administration detected among the dogs was suppression of cortisol secretion. Other changes that typically develop with iatrogenic hyperadrenocorticism (eg, increased serum alkaline phosphatase activity) were not apparent.²⁴ Thus, administration of glucocorticoids at high doses or for long periods (or both), which results in greater systemic effects, appears to be required for suppression of aldosterone secretion. Further studies are required to determine the dosage and duration of glucocorticoid treatment needed to achieve that effect.

Another limitation of the present study was the small number of dogs in each group. The study was designed to determine whether a difference in serum aldosterone concentration could be detected between dogs that were treated with prednisone and those that were not. On the basis of an estimated 50% decrease in ACTH-stimulated serum aldosterone concentration as a result of prednisone treatment and the expectation that data would be nonparametric, sample size was calculated to be 5 (assuming that the type I error was 0.05 and the power was 0.8 with an accepted error of 0.1).

In the present study, hypochloremia developed in clinically normal dogs during administration of prednisone at anti-inflammatory dosages. On occasion, dogs may be suspected of having developed naturally occurring hypoadrenocorticism during glucocorticoid treatment. To determine whether complete adrenocortical insufficiency (which is typical in cases of spontaneous hypoadrenocorticism) is present in those dogs, clinicopathologic evaluations for expected electrolyte abnormalities are often performed. However, the results of the present study indicate that such practice is inappropriate because marked hypochloremia may be present in the face of normal serum aldosterone concentration and aldosterone secretory capacity in dogs receiving exogenous glucocorticoid treatment. In addition, if a patient is tested for hypoadrenocorticism after cessation of glucocorticoid treatment, decreased ACTH-stimulated serum aldosterone concentration cannot be used as evidence of spontaneous disease. The mechanism and clinical importance of the changes remain to be determined. Lastly, dogs that have signs of a hypoadrenal crisis shortly after cessation of glucocorticoid treatment may benefit from mineralocorticoid administration because their mineralocorticoid secretory reserve may be diminished.

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