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Echocardiographic Assessment of Hemodynamic Changes Produced by Two Methods of Inducing Fluid Deficit in Dogs

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Background: Hydration status is important to the cardiovascular system because of its effects on preload. Decreased preload can alter echocardiographic measurements of systolic and diastolic function, potentially confounding interpretation of results.

Hypothesis/Objectives: Mild fluid deficits are associated with measurable echocardiographic changes that are validated by physical and biochemical markers of decreased intravascular volume.

Animals: Twenty-five healthy staff/student-owned dogs with no evidence of cardiac or renal disease.

Methods: Prospective, interventional laboratory study. Dogs were randomly assigned to water deprivation (WD) alone for 8 hours (n = 13) or to furosemide treatment (FTx, 2.5 mg/kg IV) followed by WD for 8 hours (n = 12). Echocardiograms, biochemical sampling, and physical parameters were measured at baseline, and after 4 and 8 hours.

Results: Both protocols induced fluid deficit as indicated by significant ($P < .00001$) decreases in weight at 4 hours (WD, 1.1%; FTx, 3.7%) and 8 hours (WD, 2.7%; FTx, 4.5%). Furosemide significantly decreased left ventricular end-diastolic volume (54.3 ± 19.3–42.1 ± 17.3 mL, $P < .0001$), cardiac index (4.2 ± 1.1–2.9 ± 0.9 L/min/M^2, $P < .0001$), and mitral valve E wave velocity (0.79 ± 0.2–0.66 ± 0.2 m/s, $P = .0004$). These changes were accompanied by significant increases in blood urea nitrogen concentration (13.8 ± 2.6–14.8 ± 2.7 mg/dL, $P = .04$), vasopressin concentration (1.4 ± 1.2–3.3 ± 1.9 pg/mL, $P = .045$), and PCV (49.8 ± 4.5–53.2 ± 6.5%, $P = .006$). Effects of water deprivation alone were similar, but less pronounced.

Conclusions and Clinical Importance: Mild fluid deficits have measurable hemodynamic effects in dogs. Hydration status should be considered when evaluating cardiac function by echocardiogram.

Key words: Echocardiography; Hemodynamics; Physiology; Vasopressin ADH.

The terms dehydration and volume depletion are commonly used interchangeably, but in fact, have very different meanings. Dehydration signifies the loss of pure water and, if access to water is denied or water intake is inadequate, hypernatremia ensues.[1,2] Volume depletion is more properly termed "extracellular volume depletion" and is because of loss of both sodium and water from the body.[1] Although there have been numerous studies of dogs evaluating the effects of water deprivation, they have focused primarily on its biochemical consequences, with only minor attention to the hemodynamic effects.[3–6] Conversely, most studies of volume depletion have centered on hemodynamics, with little attention to the biochemical responses. The hemodynamic response to volume depletion is consistent.[7–10] The most common observation is a reduction in the cardiac chamber dimensions during diastole, with variable affects on systolic dimensions, wall thicknesses, and Doppler-derived measurements of blood flow and tissue movement.

The overall prevalence of mild to moderate fluid deficit in dogs presenting for cardiac evaluation is unknown, but is likely common. Dehydration in dogs can occur for a variety of reasons, including owners withholding water during travel, refusal to drink because of anxiety, loss of water from panting, limited access to water during diagnostic procedures, and in some dogs, increased metabolism. Volume depletion occurs secondary to a variety of abnormalities, including blood loss, vomiting, diarrhea, and 3rd space losses. Fluid deficits, and in particular volume depletion, have the potential to confound evaluation of the cardiovascular system because of their effects on preload and subsequent cardiac changes.

The purpose of this study was to compare the hemodynamic and biochemical effects of 2 different methods of inducing mild fluid deficits in clinically normal dogs, and determine if the changes are sufficient to mimic cardiac pathology.

Abbreviations:

AVP	arginine vasopressin
BUN	blood urea nitrogen
FTx	furosemide treatment group
LA	left atrium
LVEDV	left ventricular end-diastolic volume
PRA	plasma renin activity
SBP	systolic blood pressure
USG	urine specific gravity
WD	water deprivation

Materials and Methods

Animals

Dogs were recruited from among the staff and students at the Veterinary Medical Teaching Hospital, University of Missouri. Dogs were determined to be healthy based on normal physical

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examinations, echocardiograms, and biochemical evaluations. All dogs were fasted for 12 hours before enrollment in the study, but were allowed free access to water until the baseline measurements were made. All animals participated in the study with signed owner consent, and the study was approved by the University of Missouri's Animal Care and Use Committee.

Study Design

Dogs were randomly assigned to receive either furosemide treatment, 2.5 mg/kg IV, followed by water deprivation for 8 hours (FTx group; n = 12), or water deprivation alone for 8 hours (WD group; n = 13). Furosemide was administered immediately after completion of the baseline measurements. In both groups, all measurements were repeated at 4 and 8 hours. Dogs were brought into the study room and allowed to acclimate for 10 minutes before data collection at each time point.

Clinical evaluation included the following parameters: weight, heart rate, and blood pressure. Systolic blood pressure (SBP) was determined as the mean of 3–5 readings by the Doppler method.[a] Heart rate was obtained by auscultation before performing the blood pressure measurements. Weight was measured after each subject had urinated, with the same scale at each time point.

Biochemical Evaluation

Blood was collected into lithium heparin tubes for measurement of blood urea nitrogen (BUN), creatinine, sodium, potassium, chloride, PCV, and total protein. Samples were assayed within 30 minutes of sample collection, and analyses were performed by the Veterinary Medical Diagnostic Laboratory, University of Missouri. A free-catch urine sample was obtained for measurement of urine specific gravity (USG), sodium and potassium concentration, and osmolality. Urine and plasma samples were frozen at −80°C and subsequently analyzed for osmolality with a vapor pressure osmometer.[b] Blood samples for assay of arginine vasopressin (AVP) and plasma renin activity (PRA) were drawn into prechilled 3 mL EDTA tubes, immediately placed into ice, centrifuged at 6°C, and then stored frozen at −80°C. The samples were submitted frozen on dry ice to the testing laboratories for assay.[c,d] Renin activity in plasma was measured by radioimmunoassay using a modification of Haber et al[11] with angiotensin I standards, tracer, and antibody from the National Bureau of Standards, Perkin Elmer Life Sciences, and Arnel, respectively. Plasma samples for AVP assay were extracted as described previously.[12,13] The dried samples were reconstituted in assay buffer and radioimmunoassay performed in duplicate as reported previously.[14] Assay sensitivity was 0.1 pg/assay tube and 50% displacement was 3.8 pg/tube. Intra- and interassay variabilities were 7 and 13.4%, respectively.

Echocardiography

All examinations were performed by a single echosonographer (H.E.D.). Two-dimensional, M-mode, and Doppler echocardiographic examinations were performed utilizing standard views in unsedated dogs.[15–17] Left ventricular short-axis area was measured from a right-parasternal view by tracing the endocardial borders, and excluding the papillary muscles. Three to 6 consecutive cycles were measured and averaged for each variable. Images were recorded and stored for measurement at a later date. All measurements were performed by a separate examiner (D.M.F.). Complete blinding to the subject ID was not possible because of the presence of a computer encoded time-date stamp on all images. However, the order in which the studies were measured was performed randomly to limit bias.

Statistical Analysis

All calculations were performed with a commercial statistical software package.[e] Values are given as mean ± standard deviation. Results within each group were analyzed by one-way repeated measures analysis of variance. When indicated, post hoc analysis was performed by the Tukey-Kramer multiple comparison test to determine which time points were significant. Results obtained at 4 and 8 hours were compared with control at time 0, but not each other. The baseline values of the 2 groups were compared by 2-sample *t*-tests. A P-value $< .05$ was accepted as significant.

Results

There was no significant difference in age between the FTx and WD groups, 4.0 ± 2.3 versus 4.5 ± 3.5 years, respectively ($P = .62$); or weight, 29.4 ± 10.1 versus 25.8 ± 7.8 kg, respectively ($P = .36$). Sex distribution in the FTx group included 6 females (3 neutered) and 6 males (4 neutered); the WD group included 5 neutered females and 8 neutered males, $P = .16$. The majority of dogs in both groups were Labrador Retrievers and mixed breed dogs.

There were no differences between the FTx and WD groups in any of the baseline biochemical or clinical parameters (Tables 1 and 2). There were significant increases in BUN, creatinine, sodium, PCV, total protein, plasma osmolality, urine sodium concentration, PRA, and AVP (Table 1). There were significant decreases in weight, potassium, chloride, USG, urine osmolality, and urine potassium concentration. SBP and heart rate were unchanged by furosemide administration. The biochemical and clinical effects of 8 hours of water deprivation alone were modest (Table 2). There were significant decreases in BUN, creatinine, and weight, whereas AVP and urine sodium concentration were the only parameters to show a significant increase.

There were no differences between the FTx and WD groups in any of the baseline echocardiographic parameters (Tables 3 and 4). FTx caused significant decreases in the two-dimensional left atrium (LA) dimension, left ventricular end-systolic volume and left ventricular end-diastolic volume (LVEDV), stroke volume, M-mode LV diastolic diameter, E wave velocity and transmitral filling velocity slope, LV short-axis area in systole and diastole, aortic peak pressure gradient, and cardiac index (Table 3). Only the two-dimensional LA size and the LVEDV measurements were significantly decreased by water deprivation (Table 4). Neither protocol induced significant changes in septal or LV free-wall dimensions (data not shown).

Discussion

Both protocols resulted in a significant decrease in the mean body weight 4 and 8 hours after the baseline evaluation. Not surprisingly, the average decrease was more profound in the FTx group than in the WD group (4.5 versus 2.7%, respectively). Biochemical parameters were affected by furosemide administration in a manner that was generally predictable. Although furosemide typically causes hyponatremia, plasma sodium concentration was increased in our dogs. This occurred because the sodium concentration in urine was less than that of the plasma,

Table 1. Physical and biochemical (mean ± SD) effects of furosemide (IV) on healthy dogs (n = 12) at baseline, and 4 and 8 hours after treatment.

FTx Group	Baseline	4 Hours	% Change 0–4	8 Hours	% Change 0–8	*P*-Value[†]
Weight (kg)	25.8 ± 7.9	24.9 ± 7.4	−3.7	24.7 ± 7.6	−4.5	< .0001
SBP (mmHg)	125.0 ± 14.4	126.8 ± 18.9	1.4	126.1 ± 17.8	0.9	.91
Heart rate (bpm)	111.3 ± 20.2	112.0 ± 17.7	0.6	105.3 ± 15.1	−5.4	.28
BUN (mg/dL)	13.8 ± 2.6	14.4 ± 2.7	4.2	14.8 ± 2.7	7.2	.0002
Creatinine (mg/dL)	0.92 ± 0.1	1.01 ± 0.1	10.0	1.03 ± 0.2	11.8	< .0001
Sodium (mEq/L)	146.5 ± 1.6	148.0 ± 2.4	1.0	148.2 ± 2.1	1.1	.003
Potassium (mEq/L)	4.1 ± 0.2	3.7 ± 0.3	−8.6	3.8 ± 0.2	−6.4	.0006
Chloride (mEq/L)	112.8 ± 1.5	109.6 ± 1.6	−2.8	109.5 ± 1.8	−2.9	< .0001
PCV (%)	49.8 ± 4.5	52.5 ± 7.3	5.5	53.2 ± 6.5	6.8	.006
Total protein (g/dL)	7.0 ± 0.6	7.8 ± 0.5	11.1	8.0 ± 0.6	13.8	< .0001
Urine specific gravity	1.032 ± 0.01	1.013 ± 0.01	−1.8	1.027 ± 0.01	−0.5	< .0001
Urine [Na^+] (mEq/L)	58.8 ± 42.4	113.7 ± 9.1	93.4	58.6 ± 37.4	−0.34	.001
Urine [K^+] (mEq/L)	123.5 ± 65.6	54.2 ± 23.8	−56.1	77.2 ± 28.9	−37.5	.0009
Posm (mOsm/kg)	315.2 ± 3.4	322.5 ± 10.9	2.3	319.5 ± 9.3	1.4	.05
Uosm (mOsm/kg)	1117.3 ± 536	549.8 ± 200	−50.8	946.6 ± 211	−15.3	.0001
PRA (ng A1/mL/h)	1.65 ± 1.1	5.07 ± 1.5	207.9	4.88 ± 2.9	196.9	.0005
AVP (pg/ml)	1.39 ± 1.2	2.24 ± 1.1	61.4	3.35 ± 1.9	140.6	.045

[†]*P*-value for the entire ANOVA including baseline, 4, and 8 hours. Highlighted cells indicated where the results were significantly different from baseline on post-hoc analysis, $P < .05$.

AVP, arginine vasopressin; BUN, blood urea nitrogen; [K^+], potassium concentration; [Na^+], sodium concentration; SBP, systolic blood pressure; Posm, plasma osmolality; PRA, plasma renin activity; Uosm, urine osmolality; FTx, furosemide treatment; SD, standard deviation.

and hypernatremia results if access to water is restricted.[18] Both USG and osmolality were decreased at one or both time points because of the inhibition of renal concentrating ability seen with loop diuretics.[19] Other indicators of hemoconcentration in the FTx group included increased BUN, creatinine, PCV, total protein, and plasma osmolality.

Water deprivation alone resulted in an average of almost 3% body weight reduction after 8 hours; however, this was accompanied by relatively few other changes in biochemical or clinical parameters. Urine sodium concentration was significantly increased by 8 hours. Whereas it might be expected that the sodium excretion would be decreased as a mechanism to maintain extracellular fluid volume, the phenomenon of dehydration-induced, vasopressin-associated natriuresis is well described, serving as a defense for preventing hypertonicity.[5,6,20,21] Creatinine and BUN both showed small, but significant declines by 8 hours. Whereas this appears counterintuitive, similar results were seen when healthy dogs were water deprived for periods that ranged from 30 to 96 hours.[3] The mechanism of this decrease is unknown, but may result from

Table 2. Physical and biochemical (mean ± SD) effects of 8 hours of water deprivation on healthy dogs (n = 13) at baseline, and after 4 and 8 hours of deprivation.

WD group	Baseline	4 Hours	% Change 0–4	8 Hours	% Change 0–8	*P*-Value[†]
Weight (kg)	29.4 ± 10.1	29.1 ± 9.9	−1.1	28.57 ± 9.7	−2.7	< .0001
SBP (mmHg)	124.2 ± 13.6	126.6 ± 18.7	2.0	122.1 ± 19.8	−1.7	.44
Heart rate (bpm)	101.1 ± 24.7	97.5 ± 22.1	−3.6	96.2 ± 18.0	−4.8	.28
BUN (mg/dL)	16.1 ± 9.1	14.9 ± 8.6	−7.7	13.1 ± 5.5	−18.7	.04
Creatinine (mg/dL)	0.98 ± 0.2	0.92 ± 0.2	−6.3	0.89 ± 0.2	−8.7	.008
Sodium (mEq/L)	145.8 ± 2.7	146.1 ± 2.5	0.2	146.0 ± 3.5	0.2	.92
Potassium (mEq/L)	4.1 ± 0.5	4.1 ± 0.3	−0.9	4.0 ± 0.2	−3.4	.69
Chloride (mEq/L)	113.4 ± 2.2	113.6 ± 1.7	0.2	113.9 ± 2.6	0.5	.62
PCV (%)	46.9 ± 4.3	46.0 ± 4.3	−2.6	45.6 ± 4.7	−2.8	.16
Total protein (g/dL)	6.8 ± 0.5	6.8 ± 0.4	−0.8	6.9 ± 0.5	1.7	.93
Urine specific gravity	1.029 ± 0.01	1.033 ± 0.01	0.4	1.035 ± 0.01	0.5	.31
Urine [Na^+] (mEq/L)	69.8 ± 53.5	111.0 ± 69.9	59.1	141.8 ± 63.3	103.4	.005
Urine [K^+] (mEq/L)	93.3 ± 50.4	101.0 ± 43.6	8.2	111.3 ± 58	19.2	.13
Posm (mOsm/kg)	317.1 ± 5.0	315.3 ± 4.5	−0.6	313.6 ± 3.5	−1.1	.06
Uosm (mOsm/kg)	1112.5 ± 570	1237.9 ± 347	11.3	1280.1 ± 320	15.1	.26
PRA (ng A1/ml/h)	1.49 ± 1.2	1.10 ± 0.7	−25.1	1.33 ± 0.8	−10.4	.37
AVP (pg/mL)	0.68 ± 0.6	1.15 ± 0.9	69.0	2.22 ± 2.1	227.5	.05

[†]*P*-value for the entire ANOVA including baseline, 4, and 8 hours. Highlighted cells indicated where the results were significantly different from baseline on post-hoc analysis, $P < .05$.

See Table 1 for abbreviations.

Table 3. Results of furosemide (IV) on echocardiographic parameters (mean ± SD) in healthy dogs (n = 12) at baseline, and after 4 and 8 hours of deprivation.

FTx group	Baseline	4 Hours	% Change 0–4	8 Hours	% Change 0–8	*P*-Value[†]
2D LA (cm)	3.39 ± 0.4	3.22 ± 0.5	−5.1	3.18 ± 0.5	−6.2	.013
LVEDV (mL)	54.32 ± 19.3	44.27 ± 17.2	−18.5	42.14 ± 17.3	−22.4	< .0001
LVESV (mL)	18.12 ± 9.8	15.65 ± 8.1	−13.6	14.86 ± 9.0	−18.0	.018
Stroke volume (mL)	36.21 ± 10.5	28.62 ± 10.0	−21.0	27.27 ± 9.7	−24.7	< .0001
MM LA (cm)	2.64 ± 0.4	2.48 ± 0.3	−6.1	2.49 ± 0.4	−5.5	.19
MM LA/Ao	1.21 ± 0.2	1.13 ± 0.1	−6.8	1.12 ± 0.2	−7.6	.21
MM LVIDd (cm)	3.80 ± 0.6	3.53 ± 0.6	−7.0	3.65 ± 0.6	−3.8	.0038
MM LVIDs (cm)	2.50 ± 0.5	2.39 ± 0.5	−4.3	2.44 ± 0.5	−2.3	.56
MFV E wave (m/s)	0.79 ± 0.2	0.68 ± 0.2	−13.5	0.66 ± 0.2	−16.7	.0004
MFV A wave (m/s)	0.64 ± 0.2	0.60 ± 0.2	−5.7	0.55 ± 0.2	−14.6	.07
MFV slope (m/s^2)	6.61 ± 2.8	4.43 ± 1.5	−32.9	4.89 ± 1.8	−25.9	.004
LV SAAd (cm^2)	12.37 ± 3.2	10.49 ± 3.6	−15.2	10.34 ± 3.7	−16.4	< .0001
LV SAAs (cm^2)	5.01 ± 2.2	4.29 ± 2.2	−14.3	4.40 ± 2.2	−12.1	.015
Aortic PG (mmHg)	7.16 ± 2.3	5.86 ± 2.7	−18.2	4.91 ± 2.3	−31.5	.003
CI ($L/min/M^2$)	4.20 ± 1.1	3.34 ± 0.8	−20.6	2.94 ± 0.9	−29.9	< .0001

[†] *P*-value for the entire ANOVA including baseline, 4, and 8 hours. Highlighted cells indicated where the results were significantly different from baseline on post-hoc analysis, $P < .05$.

2D, two-dimensional; CI, cardiac index; LA, left atrium; LA/Ao, left atrial to aortic root ratio; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; MFV, transmitral filling velocity; MM, M-mode; PG, pressure gradient; SAAd, short-axis area in diastole; SAAs, short axis area in systole; FTx, furosemide treatment; SD, standard deviation.

fluid shifts from the interstitium, as both studies also showed a tendency for PCV to decline. In our study, urine osmolality and USG increased over time in the WD group, but the change was not significant. This was not unexpected given that the time to maximal USG averaged 40 hours.[3]

PRA was significantly increased at 4 and 8 hours in the FTx group, and AVP concentration was significantly increased in both treatment groups at 8 hours. Numerous studies of dehydration, extracellular volume depletion, and mechanically decreasing preload have shown these manipulations to be potent stimulators of renin and AVP release in dogs.[5,6,20,22] Notably, PRA increased substantially in response to volume depletion in the FTx group whereas there was no significant change in PRA with water deprivation alone. This is because of the more profound effects of furosemide on intravascular volume compared with the effects of pure dehydration. Renal hypoperfusion is one of the major physiologic stimuli of renin release.[23] In contrast, both groups displayed significant increases in AVP. AVP is also released in response to hypovolemia; however, the AVP secretory response is more sensitive to changes in plasma osmolality.[24] In 1 study, significant increases in AVP concentration and plasma osmolality were shown after just 2 hours of water deprivation in dogs.[6] Both of these

Table 4. Results of eight hours of water deprivation on echocardiographic parameters (mean ± SD) in healthy dogs (n = 13) at baseline, and after 4 and 8 hours of deprivation.

WD Group	Baseline	4 Hours	% Change 0–4	8 Hours	% Change 0–8	*P*-Value[†]
2D LA (cm)	3.68 ± 0.6	3.55 ± 0.6	−3.6	3.44 ± 0.7	−6.6	.018
LVEDV (mL)	62.27 ± 8.15	59.39 ± 9.7	−4.6	59.09 ± 4.4	−5.1	.039
LVESV (mL)	23.60 ± 9.729	21.48 ± 9.6	−9.0	21.43 ± 9.6	−9.2	.15
Stroke volume (mL)	38.67 ± 15.1	37.91 ± 13.4	−2.0	38.76 ± 13.2	0.2	.87
MM LA (cm)	2.78 ± 0.5	2.77 ± 0.4	−0.3	2.69 ± 0.5	−3.0	.57
MM LA/Ao	1.21 ± 0.2	1.25 ± 0.2	3.4	1.15 ± 0.2	−4.7	.21
MM LVIDd (cm)	3.92 ± 0.6	3.95 ± 0.7	0.9	3.89 ± 0.7	−0.7	.71
MM LVIDs (cm)	2.69 ± 0.6	2.83 ± 0.6	5.4	2.73 ± 0.6	1.5	.10
MFV E wave (m/s)	0.75 ± 0.2	0.75 ± 0.2	−0.2	0.81 ± 0.2	8.0	.19
MFV A wave (m/s)	0.56 ± 0.1	0.52 ± 0.1	−6.6	0.58 ± 0.2	3.2	.33
MFV slope (m/s^2)	5.56 ± 2.3	5.40 ± 1.8	−2.9	5.51 ± 1.6	−0.9	.94
LV SAAd (cm^2)	13.89 ± 3.6	13.53 ± 4.0	−2.5	13.64 ± 3.9	−1.8	.60
LV SAAs (cm^2)	6.87 ± 2.2	6.59 ± 2.7	−4.1	6.45 ± 2.4	−6.2	.25
Aortic PG (mmHg)	7.93 ± 3.6	8.33 ± 4.1	5.0	9.39 ± 5.0	18.4	.31
CI ($L/min/M^2$)	3.37 ± 1.0	3.54 ± 1.0	4.9	3.16 ± 0.9	−6.2	.20

[†] *P*-value for the entire ANOVA including baseline, 4, and 8 hours. Highlighted cells indicated where the results were significantly different from baseline on post-hoc analysis, $P < .05$.

See Table 3 for abbreviations.

parameters, along with PRA, remained elevated during 24 hours of water deprivation. However, in another study 12 hours of water deprivation had no effect on AVP concentration, but did cause a significant decrease in plasma osmolality in dogs.[4] The reason for the disparity between these studies is unknown, but may be because of differences in the sodium content of the diets, and the use of a fast before sample collection in one of the studies.

Furosemide therapy induced reductions in diastolic echocardiographic measurements, indicating a decrease in preload. These changes were often accompanied by concomitant decreases in the systolic parameters and consequently there were no significant changes in the ejection fraction, fractional shortening, or LV short-axis shortening area (data not shown). A similar study of furosemide-induced volume depletion in cats also demonstrated decreases in the LV systolic and diastolic dimensions, with no change in fractional shortening.[8] In cats, these changes were accompanied by significant increases in the diastolic septal and LV free-wall dimensions. This was not seen in our study; however, a more aggressive furosemide dosing protocol was used in that study. A human study utilizing a relatively low-dose of intravenous furosemide showed a decrease in the LV diastolic dimensions without a change in systolic dimensions, or increase in the wall thickness measurements.[7] Human subjects undergoing kidney dialysis showed significant decreases in both the systolic and diastolic LV chamber dimensions, without a change in fractional shortening or septal wall thickness.[27] Fluid removal in those individuals was ~4%, comparable to that seen in our furosemide treated dogs. Phlebotomized pigs that were subjected to 30% removal of their calculated blood volume showed marked reductions in all measurements of chamber size.[9] Similar to the furosemide treated cats, chamber reduction was accompanied by significant increases in wall thickness. This pattern is referred to as ''pseudohypertrophy,'' and appears to be a marker of more severe hypovolemia.[25] Although hypertrophic cardiomyopathy is rare in the dog, it is well described.[26,27] A dog with volume depletion sufficient to result in pseudohypertrophy could erroneously be diagnosed with hypertrophic cardiomyopathy.

Doppler estimates of diastolic function demonstrated that furosemide therapy, but not water deprivation alone, resulted in significant decreases in the transmitral E wave velocity and filling velocity slope. Doppler studies in humans have demonstrated similar results when using either the Valsava maneuver or nitroglycerin to reduce preload.[10,28] Transmitral filling velocities are very preload dependent, which is an important limitation to their use in estimating diastolic function. A dog with little or no cardiac disease may be erroneously interpreted as having a relaxation abnormality if sufficiently volume depleted. Conversely, an outflow tract obstruction in a dog with mild disease may not be detected in the presence of a fluid deficit. The diagnosis of mild subaortic stenosis in dogs is generally accepted if the flow velocity exceeds 2.25 m/s.[29] FTx in our study resulted in a 30% decrease in the aortic pressure gradient. A similar diminution in a dog with mild subaortic stenosis would result in the conclusion that the animal was normal.

The effects of 8 hours of water deprivation on echocardiographic measurements were modest. Only the two-dimensional LA size and the LVEDV were significantly decreased. This demonstrates the profound difference between the hemodynamic effects of dehydration and volume depletion. The difference in weight loss between the 2 groups was $<2\%$, but the magnitude of changes in the FTx group was comparatively striking. Although the circulating volume is reduced in states of pure dehydration, the subsequent increase in oncotic pressure tends to minimize further losses. Nonetheless, the failure to achieve a similar weight reduction in both groups must be considered a limitation of this study. Ideally, the WD group should have been followed until a similar degree of weight loss had occurred in order to make the interventions more comparable.

Other limitations must be acknowledged. Ideally, samples for neurohormone assay should have been obtained through a preplaced jugular catheter as factors not directly related to the regulation of volume or osmolality may increase their secretion. In particular, AVP secretion will increase in response to stress or pain. Although the study subjects were pets and accustomed to being handled, we cannot rule out the possibility that the increase in neurohormones was a stress response. However, the baseline AVP values were comparable to those seen in chronically instrumented dogs.[30] Additionally, the volume of blood removed at each sampling interval (~5–6 mL) should ideally have been replaced by an equal volume of crystalloid. However, in the absence of a jugular catheter, this was not practically feasible. Additionally, there was no attempt to standardize the prestudy diet with respect to the sodium load. Although there was no difference in the mean $[Na^+]$ between the 2 groups, the WD group's baseline $[Na^+]$ ranged from 141 to 151 mEq/L, whereas the baseline $[Na^+]$ in the FTx group varied by only 5 mEq/L. Although this difference is minor, it might have impacted how they responded to fluid deficit induction.

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Footnotes

[a] Parks Medical Electronics Inc, model 811B, Aloha, OR
[b] Wescor Inc, Logan, UT
[c] John D. Dingell VA Medical Center, Detroit, MI
[d] Radioimmunoassay Laboratory, University of Mississippi Medical Center, Jackson, MS
[e] NCSS, Kaysville, UT

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