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Assessment of tear film osmolarity using the TearLab™ osmometer in normal dogs and dogs with keratoconjunctivitis sicca

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Abstract

Objective To evaluate repeatability and reproducibility of tear osmolarity measured using the TearLab™ osmometer in normal dogs and to assess its diagnostic potential in dogs with keratoconjunctivitis sicca (KCS).

Animals studied Beagle dogs; six normal and five with KCS.

Procedures Tear osmolarity and Schirmer tear test-1 (STT-1) values were obtained at various times. Normal dogs were assessed for diurnal variation and repeatability and reproducibility of measurements. Dogs with KCS were evaluated before and after 5 months' topical twice-daily therapy with 2% cyclosporine.

Results Mean ± SD tear osmolarity (mOsm/L) was significantly higher in normal dogs (337.4 ± 16.2) than in dogs with KCS before therapy (306.2 ± 18.0; $P < 0.0001$), but not following therapy with 2% cyclosporine (330.5 ± 13.7; $P = 1.00$). Osmolarity readings lower than 325.5 mOsm/L were suggestive of KCS (84.8% sensitivity and 87.1% specificity). In normal dogs, tear osmolarity readings were stable during the daytime ($P = 0.99$). Repeated measurements revealed high variability and typically poor-to-moderate repeatability and reproducibility, although this was improved by taking three successive measurements at each session. Considering combined data from all dogs, a positive correlation existed between STT-1 and tear osmolarity measurements (Pearson's correlation test, $P = 0.04$, $r = 0.62$).

Conclusions Canine tear osmolarity as determined by TearLab™ osmometer was variable, required multiple readings to be informative, and differed from values reported for humans. Dogs with KCS had a lower tear osmolarity than did normal dogs, and this increased following cyclosporine therapy.

Key Words: diagnostic tool, dog, keratoconjunctivitis sicca, osmolarity, tear film, TearLab™

INTRODUCTION

Deficiency of the aqueous portion of the tear film, termed keratoconjunctivitis sicca (KCS), is one of the many causes of dry eye disease (DED) in humans and is the most commonly recognized form of DED in dogs. The reported incidence of KCS in the canine population ranges widely with most reports being between 0.36%[1] and 4%,[2] but with a single report of 35%.[3] In most dogs, KCS occurs secondary to immune-mediated destruction of lacrimal tissues, similar to Sjögren's syndrome in humans.[4,5] Thus, the dog represents a model of spontaneous DED that has been used to develop therapeutics for veterinary and human populations, as exemplified by trials of topical application of cyclosporine[6] and a lymphocyte function-associated antigen antagonist[7] currently under review for approval with the FDA.

Diagnosis of KCS in dogs is most commonly based on low Schirmer tear test values (<15 mm/min) and compatible clinical signs of ocular surface disease (e.g., mucoid discharge, conjunctival hyperemia, lackluster ocular surface, and in more severe chronic cases: corneal

vascularization, melanosis, keratinization, or fibrosis). A wide array of diagnostic tools is available for diagnosis of DED in humans, with tear film osmolarity being proposed as a useful test in many recent reports.[8–11] In humans, tear film hyperosmolarity is considered a pivotal pathophysiological factor in DED[12–15] and has been proposed as the single best marker of DED severity,[16] and more sensitive and specific for diagnosis and management of DED than are tear film break-up time, corneal staining, conjunctival staining, Schirmer tear test (STT) results, or meibomian gland grading.[9,17–19]

Until recently, measurement of tear film osmolarity required tear collection and *in vitro* assessment by either the freezing point depression or vapor pressure techniques.[20,21] Both methods require sophisticated and expensive laboratory equipment, are time-consuming, and are vulnerable to error due to evaporation of test samples.[22,23] A more recent technique uses electrical impedance to measure tear osmolarity.[10] The TearLab™ osmometer (OcuSense Inc., San Diego, CA, USA) assesses small volumes (nanoliters) of tears with similar analytical performance as laboratory-based osmometers.[24] However, despite its advantages, there are other considerations before this instrument can be adopted in veterinary clinics and translational research. Therefore, this study was designed to assess diurnal variation, repeatability, and reproducibility of tear osmolarity measurements in normal dogs, as well as the effect of topical therapy with cyclosporine on TearLab™ osmolarity measurements in dogs with KCS. These results will inform veterinary practitioners and ocular surface researchers regarding applicability of the TearLab™ osmometer for assessment of tear film osmolarity in dogs and the diagnostic value of tear film osmolarity in dogs with suspected KCS.

MATERIALS AND METHODS

Animals and medical therapies

Six normal female spayed beagle dogs (median age 1.26 years; range 1.25–1.29 years) and five female spayed beagle dogs with spontaneously arising KCS (median age, 7.6 years; range 6.8–9.8 years) were used in the study. Prior to inclusion, all dogs had a complete ophthalmic examination, including slit-lamp biomicroscopy, indirect ophthalmoscopy, applanation tonometry, assessment of STT-1 values, and ocular surface staining with fluorescein. Normal dogs were confirmed to have no clinical signs of ocular disease and a STT-1 $\geq$ 15 mm/min in both eyes (OU). Dogs with KCS were all affected unilaterally in the left eye (OS) with STT-1 < 10 mm/min and typical signs such as mucoid discharge, conjunctival hyperemia, and a lackluster cornea. In each case, their right eye (OD) was clinically normal and had a STT-1 result $\geq$15 mm/min. After a 2-month pretreatment period during which dogs received only twice-daily application of a lubricant ointment (Paralube Vet ointment, PharmaDerm, Floham Park, NJ, USA) OU, dogs with KCS were treated topically with one drop of 2% cyclosporine solution in corn oil (Wedgewood compounding pharmacy, Swedesboro, NJ, USA) twice-daily OU for 5 months. Normal dogs received no treatment at any time point during the study. The study was approved by the University of California-Davis Animal Care and Use Committee (protocol # 16547), and experiments were conducted in accordance with the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Vision Research.

Osmolarity measurements

All tear osmolarity measurements were performed with the OcuSense TearLab™ osmometer (OcuSense Inc., San Diego, CA, USA), using single-use test cards containing microchannels to collect tear fluid held by a pen designed to facilitate tear collection, and read in a portable unit which measured tear film osmolarity by electrical impedance. Tear samples were collected by passive capillary action from the inferior tear meniscus near the lateral canthus, with minimal manipulation of the lower eyelid (Fig. 1). On each occasion, the right eye was tested first and three repeated measurements were taken. The procedure was then repeated on the left eye. The time between two consecutive measurements on the same eye was always <1 min, and dogs were allowed to blink normally when not being tested. On each occasion, the ease of collection was subjectively assessed. Osmolarity readings displayed by the reader were recorded in mOsm/L. The measurement was repeated whenever the value was below or above the osmometer's range (275–400 mOsm/L). On one occasion, when a value below 300 mOsm/L was obtained, the test card was removed, and the collecting channel was

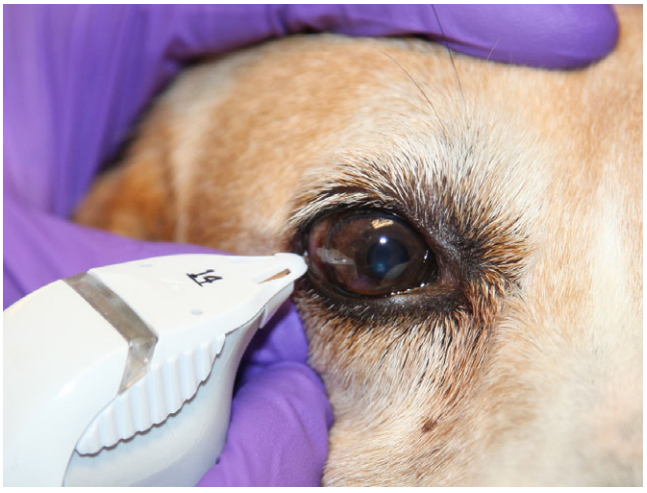

Figure 1. Tear osmolarity measurements were performed using the TearLab™ osmometer in dogs with or without KCS. Tear samples were collected from the inferior tear meniscus near the lateral canthus. The lower eyelid was kept in its natural position and minimally manipulated.

immediately examined under 40× magnification using a routine laboratory microscope.

Several precautions were taken to reduce bias and experimental effects on osmolarity measurements. All osmolarity measurements were performed in the same examination room. Both examiners (LS, SP) were trained to use the device by the same TearLab™ company representative. As directed by the manufacturer, quality control procedures were performed upon receipt of the test cards and at the beginning of each session. Ambient temperature (°C) and relative humidity (%) of the room in which testing was performed were recorded each time a measurement was made. The ambient temperature and humidity differences between any two sessions were not more than 1 °C and 5%, respectively (data not shown). Finally, no other diagnostic tests were performed and no topical medications were applied to the subject's eye for at least 12 h before osmolarity measurements. Except when evaluating diurnal variation, all osmolarity measurements were taken between 9 and 11 am.

Normal dogs—Three major outcomes were evaluated in dogs without KCS.

(1) Repeatability, that is, variation among measurements obtained from the same eye by the same investigator (LS) was evaluated for measurements taken consecutively (less than a minute apart), 30 min apart, or 24 h apart.
(2) Reproducibility, that is, variation among measurements obtained from the same eye by two different investigators (LS, SP) was evaluated for measurements taken consecutively (less than a minute apart), 30 min apart, or 24 h apart. At the first session, one of the authors (LS) always took the first set of tear osmolarity readings and the other investigator (SP) always took the second set. This order was reversed during the following session.
(3) Diurnal variation. Tear film osmolarity was measured OU by the same examiner (LS) at 8:30 AM, 11:30 AM, 2:30 PM, and 5:30 PM.

Dogs with KCS—Tear osmolarity was performed OU in dogs with KCS 1–3 times weekly during the 2-month pretreatment period, and at the completion of both therapeutic regimens. All osmolarity measurements in dogs with KCS were performed by the same examiner (SP).

Schirmer tear test (STT-1)

The STT-1 was performed by placing a standardized test strip (Merck Animal Health, Millsboro, DE) of the same lot number[25] (# 14042120) within the ventral conjunctival sac at the junction between the medial 2/3 and lateral 1/3 of the lower lid of each eye of all study dogs. Using a stopwatch to ensure a 60-s time lapse, tear production was recorded in mm/min. For normal dogs and dogs with KCS, STT-1 values were obtained 1–3 times weekly always at 8 AM and always on days other than those on which osmolarity was measured.

Repeatability and reproducibility of measurements

To provide insight into the repeatability (intra-examiner variability) and reproducibility (interexaminer variability) of tear osmolarity measurements in dogs, 95% limits of agreement (LoA) and intraclass correlation coefficient (ICC) were evaluated as previously described.[26] The ICCs were calculated using commercial 18.0 software (SPSS, Chicago, IL, USA), and values were interpreted in accordance with suggestions of Fleiss whereby values <0.4 indicate poor reliability, values ranging from 0.4 to 0.75 imply moderate reliability, and values >0.75 suggest good reliability.[27] As tear osmolarity was measured three times on each occasion, the value used for LoA and ICC determination was defined as either the first measurement per eye, the average of three measurements per eye, or the highest measurement OU. The latter two factors were reported to increase test accuracy and test-retest reliability when the TearLab™ device was used in humans.[9,18,28,29]

Statistical analysis

Data analysis was performed with commercially available software (Microsoft Excel 2007 and SPSS 18.0; SPSS 18.0 and Excel 2007, Microsoft Corporation, Redmond, WA, USA). Tear osmolarity measurements were compared between left and right eyes of normal dogs using the paired *t*-test. One-way ANOVA and *post hoc* analysis with a Bonferroni multiple comparison adjustment were used to compare the following five groups: normal dogs, unaffected eyes of dogs with KCS (before and after therapy with 2% cyclosporine), and affected eyes of dogs with KCS (before and after therapy with 2% cyclosporine). For each group, normally distributed data (as confirmed by the Shapiro–Wilk test) are presented as range and mean ± standard deviation.

Correlation between STT-1 results and tear osmolarity was assessed using Pearson product–moment correlation. Diurnal variation was analyzed with one-way ANOVA. Receiver operating characteristic (ROC) curves were used to determine the cut-off value of tear osmolarity between normal eyes and eyes with KCS. For ROC curves, tear osmolarity values from the left eye of normal dogs and the left (i.e., affected) eye of dogs with KCS prior to treatment were included. Individual values from each session were entered as single data points.

RESULTS

TearLab™ measurements were generally easily and rapidly obtained, but were subjectively more challenging in dogs with KCS than in normal dogs. In these dogs, touching the lacrimal meniscus with the TearLab™ test card was more difficult and time-consuming. The test card used on a dog with KCS and for which a tear osmolarity measurement of 299 mOsm/L was obtained was examined at 40×

magnification with light microscopy. An air bubble was noted in the collecting channel (Fig. 2).

In normal dogs ($n = 6$), no significant difference between left and right eyes was detected for STT-1 values (19.4 ± 2.3 and 19.5 ± 2.0 mm/min, respectively; $P = 0.78$) or tear osmolarity values (337.4 ± 16.2 and 337.2 ± 15.4 mOsm/L, respectively; $P = 0.93$). Therefore, data from left eyes only were used for comparisons with other groups and for further analysis of repeatability and reproducibility. In dogs with KCS ($n = 5$) clinically affected eyes had significantly lower STT-1 values (8.4 ± 4.3 mm/min) and tear osmolarity (306.2 ± 18.0 mOsm/L) than did clinically normal eyes (17.7 ± 5.0 mm/min; $P = 0.03$ and 334.5 ± 18.3 mOsm/L; $P < 0.0001$, respectively). Therefore, eyes from dogs with KCS were assigned to two separate groups: 'affected' and 'unaffected' eyes.

Descriptive data for STT-1 and tear osmolarity values are presented in Table 1. Unaffected eyes of dogs with KCS had no significant difference in tear osmolarity compared to normal dogs at any time point ($P = 1.00$). By contrast, at the start of the study (i.e., prior to treatment) tear osmolarity was significantly lower ($P < 0.0001$) in affected eyes of dogs with KCS (306.2 ± 18.0) than in normal dogs (337.4 ± 16.2 mOsm/L). However, following 5 months of treatment with 2% cyclosporine, tear osmolarity increased in the affected eyes of dogs with KCS (330.5 ± 13.7 and mOsm/L) to an extent where a significant difference with normal dogs could no longer be detected ($P = 1.00$; Table 1 and Fig. 3). Based upon ROC curve analysis, a tear osmolarity below 325.5 mOsm/L was associated with 84.8% sensitivity and 87.1% specificity for the diagnosis of KCS in dogs using the TearLab™.

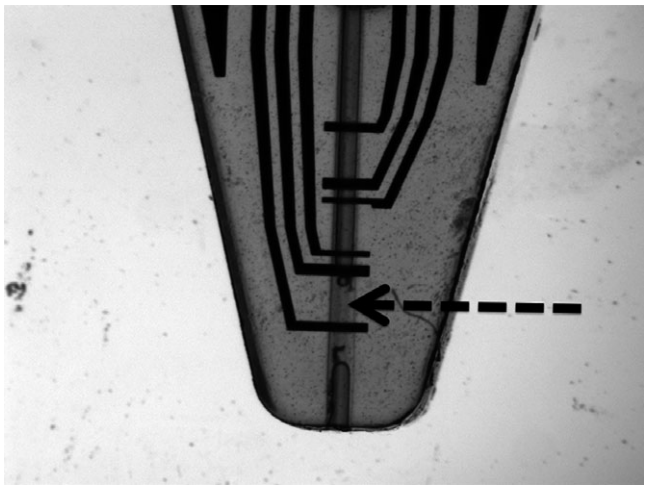

Figure 2. Presence of an air bubble (dashed arrow) in the microchip of a TearLab™ test card can be a reason for low tear osmolarity readings. This measurement was obtained from an eye with KCS (STT-1: 7 mm/min), and the value was 299 mOsm/L.

No correlation was detected between STT-1 values and tear osmolarity in normal ($P = 0.23$) or dogs with KCS ($P = 0.69$). However, a positive correlation was detected between these two tests when measurements of all dogs (i.e., normal dogs and those with KCS) were analyzed jointly ($P = 0.04$, $r = 0.62$). Tear osmolarity in normal dogs was generally stable throughout the day (8:30 am–5:30 pm), with no significant difference ($P = 0.99$) detected among mean ± SD osmolarity (mOsm/L) recorded at 8:30 am (347.0 ± 10.7), 11:30 am (347.7 ± 8.5), 2:30 pm (348.6 ± 13.1), or 5:30 pm (347.0 ± 12.7).

Considering data from a representative normal dog, repeated tear osmolarity measurements varied greatly—up to 39 mOsm/L between examiners at the same session and up to 37 mOsm/L between sessions for the same examiner (Fig. 4).

Repeatability and reproducibility data are presented in Table 2 and Table 3, respectively. Reproducibility is shown for operator LS followed by operator SP only; reversing the order (SP first, LS second) yielded similar results (data not shown). Repeatability and reproducibility experiments revealed high variability with wide 95% LoA and typically poor-to-moderate ICC (i.e., ICC < 0.75). In most cases, test–retest reliability was improved by considering only the highest value or the average of three consecutive measurements collected during each session.

DISCUSSION

While tear film hyperosmolarity is reported as a predictive attribute of DED in humans,[15] the opposite phenomenon was observed in our canine population: dogs with KCS

Table 1. Descriptive data for Schirmer tear test-1 (STT-1) and tear osmolarity values obtained from left eyes of normal dogs, and affected and unaffected eyes of dogs with keratoconjunctivitis sicca (KCS). Values for dogs with KCS were obtained prior to and following 5 months of twice-daily topical treatment with 2% cyclosporine (CsA)

Subject	Treatment	STT-1 (mm/min) (Mean ± SD)	Tear osmolarity (mOsm/L)			
			No. of readings	Mean ± SD	Range	*P* value*
Normal	None	19.4 ± 2.3	174	337.4 ± 16.2	305–390	–
KCS (unaffected eye)	None	17.7 ± 5.0	49	334.5 ± 18.3	299–374	1.00
	2% CsA	16.6 ± 4.3	55	332.1 ± 15.9	303–372	1.00
KCS (affected eye)	None	8.4 ± 4.3	44	306.2 ± 18.0	278–356	<0.0001
	2% CsA	12.5 ± 4.1	30	330.5 ± 13.7	311–360	1.00

**P* values represent comparison with untreated eyes of normal dogs.

had significantly lower tear film osmolarity (306.2 mOsm/L) compared to normal dogs with a healthy ocular surface (337.4 mOsm/L). In fact, tear osmolarity of normal dogs (337.4 mOsm/L) was comparable to that seen in humans with severe DED (336.7 mOsm/L),[9] whereas tear osmolarity of dogs with KCS (306.2 mOsm/L) was comparable to that of normal humans with a healthy ocular surface (300.8 mOsm/L).[9] Physiologically, reduced tear production is expected to cause an increased tear osmolarity as this parameter is determined mainly by the concentration of electrolytes dissolved in the aqueous phase of the tear film.[30] Although unexpected, our findings are unlikely to be due to device error as normal function of the TearLab™ osmometer used in the study was confirmed by quality control procedures performed at each session. Moreover, our study revealed a positive correlation between tear osmolarity and STT-1 testing, which is in contrast with findings of most studies in people, in which a negative correlation between these two tests exist.[31,32] A negative correlation is more physiologically explicable, as a low STT-1 value is representative of decreased aqueous tear secretion, and aqueous tear deficiency results in increased tear osmolarity.

The TearLab™ test card collects a minimal tear volume directly from the tear meniscus and is designed to minimize induction of reflex tearing. However, this was not always possible in our canine patients as touching the ocular surface was sometimes unavoidable, especially in dogs with KCS that had minimal tears. Although the time required for collection was not detailed in our study, it seemed subjectively longer in dogs with KCS compared to normal dogs; this may also have impacted our findings, as prolonged ocular contact during the tear sample collection increases tear secretion and causes a decrease in tear osmolarity.[22] In addition, and as we observed, improper sampling technique can lead to introduction of air bubbles into the TearLab™ test card, which could confound the true osmolarity measurement (manufacturer, personal communication). Overall, 20 of 44 osmolarity readings in dogs with KCS were below 300 mOsm/L. Although these may represent accurate readings, they may also be confounded by reflex tearing, air bubbles in the microchip, or

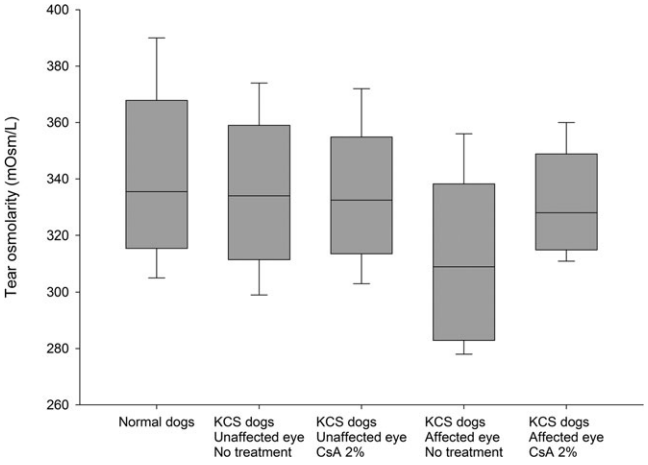

Figure 3. Tear osmolarity readings from normal dogs and dogs with KCS following or prior to treatment with 2% cyclosporine (CsA). Horizontal line within box designates the median value; lower and upper limits of box denote the first and third quartiles (i.e., 25th and 75th percentiles), respectively; upper and lower whiskers mark the maximum and minimum values, respectively.

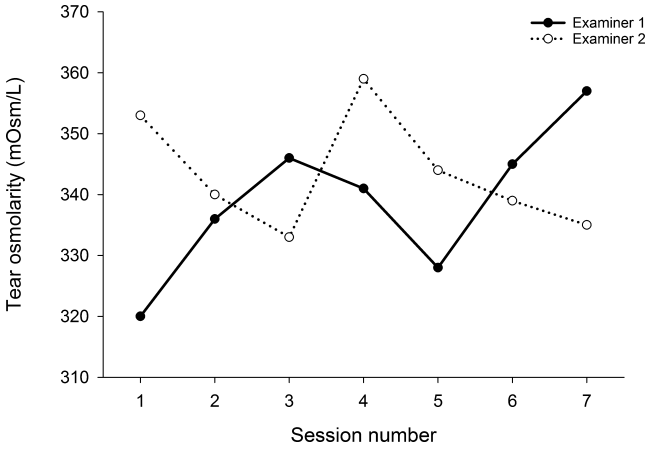

Figure 4. Repeated tear osmolarity measurements from the left eye of a representative normal dog. Note the large variability in tear osmolarity readings for the same examiner and between examiners. Sessions were separated by at least 1 day.

Table 2. Repeatability of tear osmolarity measurements in normal dogs. Measurements were obtained from six normal beagles by one investigator (LS) at different times: consecutively (less than a minute apart), 30 min apart, or 24 h apart. Limits of agreement (LoA) and intraclass correlation coefficient (ICC) are used to evaluate differences between measurements

		First readings	Highest readings	Average of three readings
Two consecutive measurements	95% LoA (mOsm/L)	−34 to +23	NA	NA
	ICC	0.49	NA	NA
30-min interval	95% LoA (mOsm/L)	−32 to +23	−25 to +16	−16 to +6
	ICC	0.31	0.69	0.71
24-h interval	95% LoA (mOsm/L)	−23 to +24	−12 to +32	−10 to +19
	ICC	0.16	0.40	0.60

NA = Not applicable. ICCs are interpreted as poor (ICC < 0.40), moderate (0.40 < ICC < 0.75), or good (ICC > 0.75) reliability.

Table 3. Reproducibility of tear osmolarity measurements in normal dogs. Measurements were obtained from six normal beagles by two investigators (LS then SP) at different times: consecutively (less than a minute apart), 30 min apart, or 24 h apart. Limits of agreement (LoA) and intraclass correlation coefficient (ICC) are used to statistically evaluate differences between measurements

		First readings	Highest readings	Average of three readings
Two consecutive measurements	95% LoA (mOsm/L)	−43 to +41	NA	NA
	ICC	0.09	NA	NA
30-min interval	95% LoA (mOsm/L)	−47 to +32	−32 to +11	−28 to +5
	ICC	−0.12	0.19	0.28
24-h interval	95% LoA (mOsm/L)	−39 to +13	−29 to +22	−22 to +9
	ICC	0.59	0.43	0.57

NA = Not applicable. ICCs are interpreted as poor (ICC < 0.40), moderate (0.40 < ICC < 0.75), and good (ICC > 0.75) reliability.

a combination of both. In addition, variability inherent to the device should be taken into consideration. Several studies using the TearLab™ have reported an inability to discriminate between human patients with DED and normal subjects,[33,34] and other publications have described a high variability in consecutive or repeated osmolarity measurements, which might be attributed to the instrument itself.[28,34]

If our findings are reflective of the true osmotic status of the canine tear film, many factors could explain the difference between tear osmolarity in humans and dogs, including species differences in pathophysiology or severity of dry eye, and influence of compensatory mechanisms on tear osmolarity. In people, DED results from a variety of causes including lacrimal failure (aqueous-deficient dry eye), increased evaporation of the tear film (evaporative dry eye), or a combination of both.[15] In dogs, the most common cause of DED is thought to be aqueous-deficient dry eye secondary to immune-mediated destruction of the lacrimal glands; a disease that shares some similarities with Sjögren's syndrome in people.[4,5,35] Reported mean ± SD tear osmolarity in Sjögren's patients has ranged from 301.9 ± 11.40 to 314.5 ± 18.0 mOsm/L;[31–33] values that are much closer to data from dogs with KCS in the present study (306.24 ± 18.01 mOsm/L). However, direct comparison is difficult because our canine patients were initially untreated while the vast majority of the human patients with Sjögren's syndrome were receiving topical and/or systemic therapeutics at the time of osmolarity testing.

It seems reasonable that differences in the pathophysiology of dry eye, disease severity at presentation, or in the extent of compensatory mechanisms also could explain, in part, the differences in observed tear osmolarity of humans and dogs. For example, people are typically examined and treated when mild or moderate symptoms of disease are first noted by the patient, whereas dogs are often presented to the veterinarian only after clinical signs become sufficiently severe to be noticeable to the owner. Compensatory mechanisms such as reflex tearing and increased blink rate in response to the ocular irritation associated with DED also reduce tear osmolarity in affected patients,[15] which can intermittently affect osmolarity measurement.[36] As a result, increased lacrimal flux and blink rate are predicted to delay the development of hyperosmolarity in evaporative dry eye, but have little influence in aqueous-deficient dry eye.[37]

In humans, normal subjects exhibit low and relatively stable tear osmolarity measurements, whereas patients with DED show elevated and more unstable readings.[38] This has led to the notion that tear film instability is a hallmark of dry eye disease. In fact, a difference in tear osmolarity of ≥10 mOsm/L between fellow eyes or between repeated measurements in the same eye is considered suspicious for DED.[38] Such a trend was not observed in our canine subjects, as normal dogs and dogs with KCS showed highly variable measurements (intra- and intersession). For instance, when the same investigator (LS) performed repeated tear osmolarity measurements on six normal dogs 1 day apart, 95% of readings between sessions differed by −23 to +24 mOsm/L (Table 2).

Two similarities were noted between tear osmolarity in people and dogs. First, normal dogs in the present study appeared to have a stable tear osmolarity profile during daytime, as shown in normal humans.[39] However, it would have been interesting to evaluate the diurnal variation in dogs with KCS, as notable diurnal variations in ocular surface physiology have been reported in people with DED.[40] Second, in both species, tear osmolarity became more normal in response to therapy, although therapy was associated with decreasing tear osmolarity in humans and increasing tear osmolarity in dogs. Sullivan and colleagues[18] showed that tear osmolarity reduced from 341 to 307 mOsm/L following 3 months' twice-daily topical application of 0.05% cyclosporine to patients with DED. In our study, 2% cyclosporine applied twice-daily OU for 5 months in dogs with KCS was associated with an increase in tear osmolarity from 306.2 to 330.5 mOsm/L.

In our study, the average of three measurements provided a stronger correlation between sessions and a better test-retest repeatability and reproducibility compared to single measurements. This is also the case in humans.[28] Some authors advocate the use of the highest osmolarity measurement of each session, derived from either repeated measures or from comparison of values from the left and right eyes.[9,18,29] From a physiological standpoint, taking into consideration the maximum measurement (and not

the average) makes more sense as the osmolarity of the diseased tear film is inherently unstable, characterized by rapid increases in osmolarity between blinks, and therefore not well characterized by a mean value. Our data in dogs showed that although averaging measurements provided slightly improved reliability (higher ICC, narrower LoA) compared to that achieved using the maximum measurement, the differences were minor. In both cases, a potential concern of repeated measures of the tear film is the risk of negatively influencing its natural state and artificially distorting osmolarity readings. However, this does not seem to be a major confounding factor, as long as the subjects are allowed to blink normally during collection.[29] Because each measurement requires a new single-use test card, the increased cost of testing in this manner must be considered, especially relative to other commonly used dry-eye tests in veterinary patients such as the STT and tear film break-up time.

CONCLUSION

The TearLab™ system is noninvasive and easy to use in dogs and quickly provides tear osmolarity readings available for immediate assessment by clinicians or researchers. Our study highlights fundamental differences between canine and human tear film osmolarity, suggesting TearLab™ would not be a predictive end point when using the dog as a model for DED in humans. The reason for this disparity is unknown, but is likely related to differences in severity and pathophysiology of DED in dogs and humans, and inherently different compensatory mechanisms in the two species. Species differences notwithstanding, the data obtained suggest the TearLab™ system is of potential use for diagnosis and management of KCS in dogs. Tear film osmolarity is able to discriminate between normal dogs and those with KCS, with values lower than 325.5 mOsm/L being suggestive of KCS regardless of the exact underlying mechanism(s). However, extensive overlap was observed between the range of tear osmolarity values in both groups. Also, repeatability of measurements was relatively poor, as shown by low ICCs, wide LoA, and large intra- and interexaminer variations. Repeatability of TearLab™ values can be improved by using the average or highest value when three measurements are taken sequentially; however, this may be cost-prohibitive (especially compared to other commonly used tear film tests) as each measurement requires a new single-use test card. Further studies are needed before tear osmolarity can be recommended for routine use in the diagnosis and management of KCS in the canine patient population.

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