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Tear production and intraocular pressure in canine eyes with corneal ulceration

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Abstract

This study aimed to evaluate changes in lacrimation and intraocular pressure (IOP) in dogs with unilateral corneal ulceration using the Schirmer tear test (STT) and rebound (TonoVet®) tonometry. IOP and STT values were recorded in both ulcerated and non-ulcerated (control) eyes of 100 dogs diagnosed with unilateral corneal ulceration. Dogs presented with other ocular conditions as their primary complaint were excluded from this study. The mean \pm standard deviation for STT values in the ulcerated and control eyes were 20.2 ± 4.6 mm/min and 16.7 ± 3.5 mm/min respectively. The mean \pm standard deviation for IOP in the ulcerated and control eyes were 11.9 ± 3.1 mmHg and 16.7 ± 2.6 mmHg respectively. STT values were significantly higher ($p < 0.000001$) in the ulcerated eye compared to the control eye while IOP was significantly lower ($p < 0.0001$). There is an increase in lacrimation and a decrease in IOP in canine eyes with corneal ulceration. The higher tear production in ulcerated eyes shows the importance of measuring STT in both eyes in cases of corneal ulceration, since this increased lacrimation may mask an underlying keratoconjunctivitis sicca only evident in the contralateral eye. The lower IOP in ulcerated eyes is likely to relate to mild uveitic change in the ulcerated eye with a concomitant increase in uveoscleral aqueous drainage. While these changes in tear production and IOP in ulcerated eyes are widely recognised in both human and veterinary ophthalmology, it appears that this is the first controlled documented report of these changes in a large number of individuals.

Keywords: Corneal ulcer; Dog, Intraocular pressure, Tear production.

Introduction

Despite being widely accepted that corneal ulceration causes an increase in tear production and a decrease in intraocular pressure (IOP) as evidenced by the values from the Schirmer tear test (STT) and tonometric measurements, there appear to be few if any reports documenting these changes in ulcerated eyes in the human or canine population. This study seeks to fill this lacuna in the ophthalmic literature by comparing the tear production and IOP of eyes with ulcerated corneas compared with the control fellow eye in dogs with unilateral corneal ulceration.

The cornea serves a major refractive function while maintaining a protective barrier between the eye and the environment (Gilger *et al.*, 2008). Despite being exposed to environmental hazards, the cornea maintains the integrity of its outer surface by continual replacement of its surface epithelium and through the provision a protective covering of the surface tear-film by the lacrimal glands. Corneal ulceration is one of the most common ocular disorders encountered in veterinary practice and a major cause of ocular pain through exposure of free trigeminal nerve endings in the superficial stroma and blindness either due to excessive scarring or through subsequent perforation of the cornea. (Gilger *et al.*, 2008).

Tear secretion is controlled by the lacrimal functional unit consisting of the ocular surface (cornea, conjunctiva, accessory lacrimal glands, and meibomian glands), the main lacrimal gland and the interconnecting innervation (sensory afferent and autonomic efferent nerves) (Stern *et al.*, 2004; Williams, 2008).

The sensory nerves derived from the ophthalmic branch of the trigeminal nerve in the cornea activate the efferent parasympathetic and sympathetic nerves originating in the parasympathetic motor nucleus of the facial nerve but travelling with the trigeminal nerve to the lacrimal gland (Marfurt *et al.*, 2001; Situ and Simpson, 2010). The functional unit regulates the major components of the tear film in order to protect the ocular surface. Painful stimulation of the eye is known to result in tear secretion and other reflexes to prevent the eye from potential damage (Unger, 1990; Belmonte *et al.*, 1997; Situ and Simpson, 2010) but there is little in the literature to show a direct link of increased tear secretion with corneal ulceration.

The IOP occurs through a balance between the production of aqueous humour and its drainage through the iridocorneal angle (conventional outflow) and through the uveoscleral pathways (unconventional outflow) (Reinstein *et al.*, 2009).

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It has been previously documented that after an initial rise in IOP following ocular surface injury, a prolonged reduction in IOP is usually found (Unger, 1990). An antidromal trigeminal reflex arc is considered to be responsible for this hypotony, predominantly caused by a prostaglandin induced increase in unconventional aqueous outflow (Camras *et al.*, 1977; Fine *et al.*, 2007). Despite this understanding of the mechanism of such a change in IOP there appear to be few if any reports in the literature, just as with tear secretion, to show a direct link between corneal ulceration and decreased IOP in the dog.

Materials and Methods

This prospective study aims to determine tear production using the STT I method and IOP by rebound tonometry using the TonoVet® (ICare, Helsinki, Finland) in canine eyes with unilateral corneal ulcers to establish the difference in the values between the ulcerated and the fellow control eye. The second eye in the same animal was used as a control to eliminate any diurnal variations of time of sampling or effects of age, gender or weight of the patient (Berger and King, 1998; Gelatt and MacKay, 1998; Hartley *et al.*, 2006).

This study was undertaken over 12 months at the Queen's Veterinary Hospital, Department of Veterinary Medicine, University of Cambridge and at 14 first opinion clinics visited by the senior author in an ambulatory referral clinic. The study was conducted in line with the regulations of the UK Veterinary Surgeons' Act 1966 and was approved by the Ethics and Welfare Committee of the Department of Veterinary Medicine.

One hundred dogs with unilateral corneal ulcers as their presenting complaint were selected for this study in order to compare values between the ulcerated eye and the non-ulcerated fellow eye acting as a control. For each subject, the breed, sex, age, duration and depth of the ulcer were recorded. Any dogs with bilateral corneal ulceration or other conditions as a presenting complaint were excluded as were animals in which either eye had significant additional pathology at presentation.

Corneal ulceration was diagnosed on the basis of a full ocular examination including the use of direct and indirect ophthalmoscopy and slit lamp biomicroscopy, with ulceration confirmed by fluorescein staining undertaken after the STT and IOP values had been obtained. Ulceration was scored as superficial (i.e. a corneal epithelial erosion), mid-stromal (extending no deeper than half stromal thickness, or deep (extending deeper than half the thickness of the stroma) but not including descemetocoeles or perforating corneal lesions. Signs of mild ocular inflammation (conjunctival hyperaemia, aqueous flare, miosis but without profound cellular infiltrative change in the eye) were recorded where present and scored as mild,

moderate or severe. Tear production was measured in both eyes using the Schirmer I test which measures aqueous production over one minute in an unanaesthetised eye, therefore measuring basal and reflex tear production (Gelatt *et al.*, 1975). Standard STT strips (EagleVision™, Schering-Plough, Memphis TN, USA) with the same batch number were used to measure tear production. IOP was measured in both eyes using the TonoVet® rebound tonometer (Icare, Helsinki, Finland) on calibration setting D (used when evaluating iop in the dog) and without the need for topical anaesthesia of the corneal surface (Leiva *et al.*, 2006).

All statistical analyses were undertaken using SPSS v19 (IBM, Armonk, USA). STT and IOP data obeyed the three sigma rule and were thus considered normally distributed, this confirmed using the Kolmogorov-Smirnov test which yielded values of $Z=1.239$, $P=0.093$ for IOP and $Z=0.886$ $P=0.413$ for STT. Values for the ulcerated eye were compared with those for the control fellow eye using a Student's T test with significance deemed to have been reached at $P=0.05$. A cumulative logit model was used to investigate the relationship between STT and IOP and ulcer depth. This model is valuable when analysing ordered categorical data (such as ulcer depth scored as 0, 1, 2 or 3) with the reduced amount of information that such data sets contain (Lee, 1992).

Each eye was entered as an individual data point, with dog ID included as a subject effect to take non-independence into account. Ulcer depth was entered as an ordinal variable from 0 (no ulcer) to 3 (deep ulcer), with STT and IOP as covariates. Given the mean value of 20 ± 3 mm/min from normal dogs in one paper from the senior author's research group (Hartley *et al.*, 2006) and 20 ± 1 mm/min in a paper from another group (Giannetto *et al.*, 2009) a power calculation showed that detecting a 3mm/min difference between ulcerated and control eyes with a statistical power of 0.8 and significance at 0.05 would require 30 cases. Similarly detecting a difference of 5mmHg in dogs with a mean and standard deviation of 19 ± 6 mmHg, a figure derived from a previous published large sample of normal dogs (Giannetto *et al.*, 2009), would require a sample size of 36 dogs. We examined 100 dogs to ensure sufficient power of the study.

Results

Signalment of cases, ulcer depth and duration, are shown in Table (1). STT results and measurements of IOP for both the ulcerated and the control contralateral eye are given in Table (2) together with scoring of conjunctival hyperaemia, a summatory score of signs of intraocular inflammation (aqueous flare, iris swelling, iris hyperaemia, hypopyon) and degree of miosis, all semi-quantitatively assessed from 0 (not present) to 3 (severe).

Table 1. Signalment and ulcer characteristics of dogs involved in study.

Case	Breed	Gender	Age	Ulcer duration (days)	Ulcer type
1	Boxer	fn	7	6	superficial
2	CKCS	mn	13	14	mid stromal
3	Cross bred	me	12	21	mid stromal
4	Cocker spaniel	mn	5	1	superficial
5	WHWT	mn	12	21	mid stromal
6	Shih Tzu	mn	5	14	superficial
7	Labrador retriever	me	0.2	2	deep stromal
8	Pug	fe	0.8	3	deep stromal
9	French bulldog	fe	4	21	superficial
10	French bulldog	me	6	12	superficial
11	Boxer	me	5	7	superficial
12	Jack Russell terrier	me	8	21	superficial
13	English springer spaniel	me	7	14	mid stromal
14	Boxer	me	12	7	superficial
15	Pug	fn	8	4	mid stromal
16	Pug	fe	0.8	2	pinpoint mid stromal
17	Boxer	mn	8	14	superficial
18	Cross bred	mn	7	12	superficial
19	English springer spaniel	mn	8	21	superficial
20	Pug	fe	6	10	pinpoint mid-stromal
21	Pug	fn	7	7	central mid stromal
22	Cross bred	mn	9	7	superficial
23	German shepherd dog	mn	11	14	superficial
24	Cairn terr	fn	13	21	superficial
25	Yorkshire terrier	mn	12	7	superficial
26	Yorkshire terrier	mn	11	7	mid stromal
27	CKCS	fn	11	7	superficial
28	Cross bred	fn	10	21	mid stromal
29	Yorkshire terrier	fn	11	7	superficial
30	Boxer	mn	12	21	superficial
31	CKCS	fn	8	7	punctuate mid-stromal
32	Pug	mn	6	5	superficial
33	SBT	mn	6	21	superficial
34	Pug	mn	4	5	superficial
35	Boxer	me	8	6	superficial
36	Shih-tzu	mn	5.5	14	superficial
37	SBTx	mn	9	7	superficial
38	Boxer	fn	7.5	10	superficial
39	Cross bred	fn	1.5	4	superficial
40	Boxer	fn	10	21	superficial
41	SBT	fn	8	28	superficial
42	Boxer	mn	8	21	superficial
43	Yorkshire terrier	fn	10	28	superficial
44	CKCS	fn	10	28	superficial
45	Sharpei	mn	3	14	superficial
46	Boxer	fn	10	21	superficial
47	SBT	fn	8	28	superficial
48	SBT	mn	7.6	100	deep stromal
49	Pug	fn	6	14	mid stromal
50	Cross bred	me	12	7	superficial
51	WHWT	Fn	8	28	sup epith + KCS
52	Pug	Fe	7.6	100	deep stromal

Table 1. Signalment and ulcer characteristics of dogs involved in study (Cont.).

Case	Breed	Gender	Age	Ulcer duration (days)	Ulcer type
53	Cross-bred	Mn	6	14	mid stromal
54	Boxer	Mn	12	7	sup ep
55	Cross-bred	Fn	13	7	mid stromal
56	CKCS	Fe	7	14	mid stromal
57	Boxer	Mn	8	21	superficial
58	SBT	Fn	10	14	mid stromal
59	Boxer	Mn	4	10	superficial
60	Pug	Fn	2	10	mid stromal
61	Boxer X	Me	9	7	superficial
62	Bulldog	Me	4	21	superficial
63	Labrador	Mn	7	21	mid stromal
64	Boxer	Mn	8	28	superficial
65	Chihuahua	Fn	3	12	mid stromal
66	Lhasa Apso	Fn	5	14	mid stromal
67	Sharpei	Fe	6	7	superficial
68	Yorkshire terrier	Mn	4	5	deep stromal
69	Boxer	Mn	8	12	superficial
70	Boxer	Mn	7	21	superficial
71	Cross bred	Me	9	28	superficial
72	Chihuahua	Fn	10	5	superficial
73	Boxer cross	Mn	11	14	superficial
74	Pug	Mn	5	7	deep stromal
75	Cross-bred	Me	12	14	superficial
76	Rotweiler	Fn	7	5	deep stromal
77	Miniature Schnauzer	Fe	6	7	superficial
78	Lhasa Apso	Fe	7	7	superficial
79	German Shepherd dog	Mn	12	14	superficial
80	Short-haired pointer	Mn	9	21	superficial
81	Boxer	Mn	8	35	superficial
82	Cross-bred	Fn	6	14	deep stromal
83	Finnish laphund	Fn	4	10	deep stromal
84	CKCS	Fe	6	6	deep stromal
85	Cocker spaniel	Fn	12	35	superficial
86	Pembroke Corgi	Me	6	5	mid stromal
87	Boxer	Mn	8	21	superficial
88	Pekingese	Me	5	2	deep stromal
89	Cross-bred	Fe	6	28	superficial
90	Boxer	Mn	8	21	superficial
91	French bulldog	Mn	5	21	deep stromal
92	Cross-bred	Fe	7	28	superficial
93	Dalmatian	Fn	9	12	superficial
94	Alaskan Malamute	Fn	7	18	superficial
95	WHWT	Mn	8	21	superficial
96	English Springer spaniel	Mn	9	25	superficial
97	Boxer	Fn	8	12	superficial
98	Yorkshire terrier	Fn	5	18	superficial
99	German shepherd dog	Fn	8	14	superficial
100	Boxer	Me	12	56	superficial

(CKCS): Cavalier King Charles Spaniel; (SBT): Staffordshire Bull Terrier; (WHWT): West Highland white terrier; (me): male entire; (mn): male neutered; (fe): female entire; (fn): female neutered.

Table 2. Intraocular pressure (IOP) and tear production measured at Schirmer tear test (STT) in ulcerated eye and normal fellow eye together with clinical data on presence (1) or absence (0) of ocular hyperaemia, clinical signs of inflammation and miosis.

Case	IOP ulcerated eye	IOP normal eye	STT ulcerated eye	STT normal eye	Conjunctival hyperaemia	Intraocular inflammation	Miosis
1	14	17	19	16	0	0	0
2	9	14	22	18	0	0	1
3	13	18	19	15	0	0	0
4	10	21	21	14	0	0	3
5	7	13	22	19	0	0	0
6	13	14	16	10	0	0	0
7	7	15	25	23	1	1	1
8	8	16	10	14	1	1	1
9	12	16	17	16	0	0	0
10	8	13	22	17	0	0	0
11	12	18	24	19	0	0	0
12	13	15	27	22	1	0	0
13	12	17	24	20	1	0	1
14	14	16	22	19	0	0	0
15	8	13	24	17	0	0	1
16	10	15	22	19	0	0	1
17	12	15	26	23	0	0	0
18	14	18	15	13	0	0	0
19	12	22	24	19	1	0	0
20	13	16	14	16	0	0	0
21	9	16	18	14	0	0	1
22	12	15	19	15	1	0	0
23	9	15	22	18	1	0	0
24	12	17	19	15	1	0	0
25	8	16	22	17	1	0	0
26	18	21	24	9	1	0	0
27	15	17	20	12	1	1	0
28	11	15	18	15	1	0	1
29	13	14	14	11	1	1	0
30	4	11	22	16	0	0	0
31	4	11	0	12	0	0	0
32	15	9	19	8	0	0	0
33	12	15	24	6	1	0	0
34	15	11	28	9	0	0	0
35	13	25	20	27	0	0	0
36	12	18	17	14	0	0	0
37	15	13	19	23	0	0	0
38	13	23	15	13	0	0	0
39	13	17	15	7	0	0	0
40	12	17	22	16	0	0	0
41	17	15	13	17	0	0	0
42	9	24	18	21	1	1	0
43	14	15	22	20	0	0	0
44	15	16	18	15	0	0	0
45	11	15	32	21	0	0	0
46	27	14	18	22	1	0	1
47	12	15	0	15	1	1	0
48	10	20	22	18	1	0	0
49	7	14	22	18	1	1	1
50	15	21	18	14	0	0	0
51	14	16	19	16	0	0	0
52	12	16	15	13	1	1	1

Table 2. Intraocular pressure (IOP) and tear production measured at Schirmer tear test (STT) in ulcerated eye and normal fellow eye together with clinical data on presence (1) or absence (0) of ocular hyperaemia, clinical signs of inflammation and miosis (Cont.).

Case	IOP ulcerated eye	IOP normal eye	STT ulcerated eye	STT normal eye	Conjunctival hyperaemia	Intraocular inflammation	Miosis
53	13	18	20	17	1	1	1
54	11	16	21	17	0	0	0
55	12	18	18	16	1	0	0
56	11	17	19	17	1	0	1
57	12	15	22	18	1	0	1
58	13	20	21	16	0	0	1
59	11	16	18	15	0	0	0
60	14	16	18	17	0	0	0
61	12	17	16	16	0	1	0
62	13	19	19	18	1	1	0
63	13	18	22	18	1	0	0
64	10	16	18	19	0	0	0
65	14	16	26	22	0	1	1
66	15	18	21	18	0	0	0
67	13	16	25	21	1	0	0
68	13	17	27	17	0	0	1
69	13	18	24	21	1	0	0
70	8	14	18	18	1	0	0
71	13	16	24	23	1	1	0
72	7	17	17	16	0	1	0
73	14	17	19	15	0	1	1
74	12	18	22	17	1	0	1
75	15	18	24	18	0	0	0
76	13	17	21	18	0	0	0
77	14	19	27	21	1	0	0
78	7	19	22	18	0	1	0
79	6	17	19	17	0	1	1
80	8	19	19	16	0	1	1
81	13	17	15	13	0	1	1
82	11	19	20	17	1	0	0
83	14	19	26	19	1	0	0
84	7	20	22	16	1	0	0
85	14	18	21	19	0	1	1
86	12	18	23	15	1	0	0
87	8	18	25	19	0	0	0
88	13	15	22	15	1	1	1
89	13	19	24	19	0	0	0
90	14	17	22	17	0	0	0
91	12	18	25	21	0	0	0
92	10	15	17	13	1	0	0
93	12	16	19	17	0	0	0
94	13	15	21	16	0	0	0
95	12	17	22	17	1	0	0
96	14	17	18	14	0	0	0
97	8	16	19	18	1	1	0
98	9	15	21	19	0	1	1
99	13	18	18	16	0	1	0
100	14	17	22	17	1	0	0

The mean (\pm standard deviation) of STT values are shown in Table (3) and the mean (\pm standard deviation) of IOP values are shown in Table (4). Both tables also show the values for eyes with superficial, mid stromal and deep stromal corneal ulcers and significance of differences between ulcerated and control eyes.

Table 3. Mean \pm Standard Deviation of Schirmer tear test (STT) values in the ulcerated and non-ulcerated eyes categorised according to the depth of the ulcer as superficial, mid stromal or deep and significance of difference in STT between ulcerated and normal eyes.

Category	Mean \pm Standard Deviation STT (mm/min)		Significance of difference
	Ulcerated	Non-ulcerated	
All ulcers (100)	20.8 \pm 4.6	16.7 \pm 3.5	P<0.000001
Superficial (68)	20.2 \pm 5.1	16.6 \pm 6.2	p<0.0001
Mid Stromal (18)	19.9 \pm 2.9	16.4 \pm 3.27	p<0.001
Deep (13)	19.0 \pm 7.9	16.7 \pm 3.9	p<0.001

Table 4. Mean \pm Standard Deviation of intraocular pressure (IOP) values in the ulcerated and non-ulcerated eyes categorised according to the depth of the ulcer as superficial, mid stromal or deep and significance of difference in IOP between ulcerated and normal eyes.

Category	Mean \pm Standard Deviation IOP (mmHg)		Significance of difference
	Ulcerated	Normal	
All Ulcers (50)	12.8 \pm 7.7	16.1 \pm 3.3	p<0.0001
Superficial (37)	12.7 \pm 2.8	16.6 \pm 2.7	p<0.00001
Mid Stromal (10)	14.1 \pm 3.8	16.2 \pm 2.2	p<0.0001
Deep (3)	7.9 \pm 1.1	17.0 \pm 1.9	p<0.0001

Mean (\pm standard deviation) STT values in the ulcerated eye compared to the non-ulcerated fellow eye were 20.8 \pm 4.6 and 16.7 \pm 3.5 respectively, this difference being highly statistically significant at p<0.000001. Mean (\pm standard deviation) values for IOP in the ulcerated eye compared to the control eye were 11.8 \pm 3.0 mmHg and 16.7 \pm 2.6 mmHg respectively, these being statistically significantly different at P=0.0001. Both IOP and STT were significant predictors of ulcer depth, with IOP significantly different at χ^2 (chi squared) = 11.25 p<0.00001 and STT significantly different at χ^2 (chi squared) = 8.28 p<0.00001. Variations in duration of ulceration did not predict differences in IOP or STT.

Discussion

The results of this study show an increased tear production and decreased IOP to occur in eyes with corneal ulceration in the dog. An increase in tear production has been noted in the literature with

reference to ocular pain (Belmonte *et al.*, 1997). One previous paper has documented that the STT in dogs with corneal epithelial defects is significantly greater when compared to the contralateral unaffected eyes (Murphy *et al.*, 2001), a result confirmed in this study, but in that report the change in tear production was but a marginal note in a larger study of superficial epithelial erosions: here we extend the investigation to a greater number of ulcerated eyes with ulcers of different types and depths. The most likely cause of increased tear production in corneal ulceration is the interaction of corneal nociceptive stimulation and subsequent lacrimal secretion (Unger, 1990).

The cornea is one of the most richly innervated tissues in the body receiving dense innervation by sensory nerves predominantly originating from neurons located in the ipsilateral trigeminal ganglion and modest sympathetic innervation from the superior cervical ganglion. The peripheral axons of the neurons terminate throughout the corneal epithelium as free nerve endings (Marfurt *et al.*, 2001). A previous study investigating the relationship between the stimulation of corneal sensory nerves and efferent output of the lacrimal functional unit determined by tear secretion showed that tear secretion increased almost linearly with the increase of stimulus intensity (Situ and Simpson, 2010). When noxious stimuli activate sensory afferents in the functional unit, a series of co-ordinated reflexes, including reflex tearing, are triggered to protect the eye from potential damage.

The current study supports previous findings that ocular pain, in this case resulting from corneal ulceration, will cause an increase in tear production due to stimulation of the lacrimal functional unit. It is possible that noxious stimuli causing the ulceration were also responsible for generating inflammation, but the ulcerated eyes did not show clinical signs of marked external inflammation which one would expect were this to be the cause of the changes in tear production and hypotony. There were no significant differences between eyes with signs of mild inflammation, as noted above, and those without.

The study makes the assumption that there is no significant difference in STT or IOP between the right and left eyes, this based on the fact that previous studies have not shown a difference between STT values of left and right eyes in normal dogs (Wyman *et al.*, 1995), and similarly IOP values have not been shown to differ between eyes (Giannetto *et al.*, 2009) so we feel confident that differences between ulcerated and control eyes here are highly likely to be related to the ulceration and not a random difference between eyes.

One limitation of this study was to only perform the Schirmer I test which measures both basal and reflex tear production. Further studies could evaluate use of the Schirmer II test to measure changes in basal tear

production in corneal ulceration, by eliminating reflex tear production. It might also be argued that for completeness the study should have evaluated the ocular aqueous outflow tract by gonioscopy, but since IOP was normal or reduced and not increased in these eyes, such an additional diagnostic step was not considered essential. It will be noted that a significant number of animals (24%) had one or both eyes in which the STT was less than 15mm/min. While impossible to prove with the current data set, it is conceivable that animals with subnormal tear production are predisposed to corneal ulceration; such a hypothesis would merit further study evaluating STT values in age and breed-matched populations with and without corneal ulceration. A decrease in IOP is well recognised in association with ocular inflammation (Fine *et al.*, 2007) but not previously associated with corneal ulceration in dogs, or indeed in any other species to these authors' knowledge. It has been noted above that IOP is formed due to a balance between the production of aqueous humour and its drainage through the uveoscleral outflow and iridocorneal angle.

Prostaglandins (PGs) are regarded as mediators of the inflammatory process and are also present in ocular tissues. Studies have shown that during ocular inflammation PG concentration in the aqueous humour is higher than that found in normal aqueous humour (Camras *et al.*, 1977). It has been shown that PGs reduce IOP in a number of animal species including dogs, cats, nonhuman primates and rabbits by increasing uveoscleral aqueous humour outflow (Nilsson *et al.*, 1989; Weinreb *et al.*, 2002).

Thus we postulate that the trigeminal antidromic reflex occurring after exposure of free stromal and intra-epithelial nerve endings following corneal ulceration results in a prostaglandin production in the anterior segment of the eye, increased unconventional aqueous outflow and a hypotony, as demonstrated in the majority of cases here. It is conceivable that changes in the ulcerated cornea such as corneal oedema alter the elasticity of the tissues and thus invalidate the rebound tonometry but recent studies suggest that such changes are small and not clinically significant (Smedowski *et al.*, 2014). The present study documents that corneal ulceration in the dog is associated with an increase in tear production and a decrease in IOP. We would suggest that the ulceration is a cause of increased lacrimation through trigeminal stimulation and reduced IOP through prostaglandin-related increase in uveoscleral outflow, but clearly these postulates cannot be proven in such an observational study. This would require an experimental protocol in which corneal ulceration was caused and lacrimation and unconventional outflow measured before and after ocular surface injury. The welfare compromise of animals used in such an investigation would be

considerable and would preclude it under UK law, but we hope that this study on eyes with spontaneous corneal ulceration has provided useful data on the ocular changes associated with corneal ulceration.

This study shows the importance of measuring tear production in both eyes of dogs with corneal ulceration since the higher tear production in the ulcerated eye may produce an apparently normal STT reading and mask an underlying case of KCS. In the current series of animals cases 6, 18, 21, 26, 27, 29, 31, 32, 33, 34 and 39 all had suboptimal STT values in the normal eye although the raised STT in the ulcerated eye would have made it appear that they did not have any deficit in tear production if only that eye had been tested. It is impossible to know if a low tear production was involved in the development of ulceration before trigeminal stimulation in the ulcerated cornea increased the STT but we consider that this may be possible. The reduction in IOP suggests a mild intraocular inflammatory process in many if not all eyes with corneal ulceration which should be documented by tonometry in any eye with an ulcerated cornea and addressed therapeutically if severe. Many facts in veterinary ophthalmology, as in many other areas of veterinary medicine, are widely accepted but without any firm data to back them up. That eyes with corneal ulceration have increased lacrimation and decreased IOP is one of these unquestioned truths. It is hoped that this study has provided some evidence to support these assumptions and also suggested areas of further research to elucidate the mechanisms by which these ocular changes occur.

Conflict of interest:

The authors declare that there is no conflict of interest.

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