Use of clinical vignette questionnaires to investigate the variation in management of keratoconjunctivitis sicca and acute glaucoma in dogs

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Abstract

There is little peer-reviewed research assessing therapeutic effectiveness in canine eye disease. Current treatments used in first opinion and ophthalmology referral practices are also somewhat poorly documented. The aim of this study was to investigate the current management of canine keratoconjunctivitis sicca (KCS) and acute primary angle-closure glaucoma (PACG) by veterinary surgeons. Questionnaires using clinical vignettes were administered to a cross section of general practitioners (‘GPs’) and veterinarians engaged in or training for postgraduate ophthalmology practice (‘PGs’). Similar treatment recommendations for KCS (topical cyclosporine, lubricant, antibiotic) were given by both groups of veterinarians with the single exception of increased topical antibiotic use by GPs. Treatment of acute glaucoma diverged between groups: PGs were much more likely to recommend topical prostaglandin analogues (PGAs) and a wider array of both topical and systemic treatments were recommended by both groups. Systemic ocular hypotensive agents were suggested infrequently. Our results suggest that treatments may vary substantially in ocular conditions, particularly in conditions for which neither guidelines nor high quality evidence exists. This study highlights the need for novel strategies to address evidence gaps in veterinary medicine, as well as for better evaluation and dissemination of current treatment experience.

Introduction

Keratoconjunctivitis sicca (KCS) and acute angle-closure glaucoma (PACG) can cause significant disability in dogs (Chester and Clark, 1987). Incidence and prevalence data for each is not well established but risks appear to be higher in some breeds and with increasing age (Gelatt and MacKay, 2004a; Sanchez and others, 2007). Veterinarians routinely encounter these and other clinical conditions for which there is limited evidence available to guide clinical decision making.
Currently there is only one veterinary pharmaceutical approved for the treatment of KCS and none for the treatment of glaucoma; it is unknown how this may affect treatment choice but could potentially result in diverse management strategies.

Numerous clinical guidelines have been developed for the treatment of human disease, in part to address unwanted treatment variation and to improve quality of care (Timmermans and Mauck, 2005). In medicine, greater treatment variation is seen for interventions which have uncertain or marginal benefit and for conditions which lack clinical guidelines (Skinner, 2011). Veterinary guidelines rely more heavily on consensus due to a small evidentiary base but areas with greater treatment uncertainty are argued to be most needful of guidance (Polzin and Cowgill, 2013). While guidelines and consensus statements now exist for a number of companion animal conditions (e.g. Atkins and others, 2009; Podell and others, 2016; Olivry and others, 2010), we are unaware of any clinical guidelines for canine ophthalmic disease.

Clinical vignette-based questionnaires are a useful way of assessing treatment patterns and variation in clinical practice; they have been used to assess adherence to guidelines and to assess factors in clinical decision-making in medicine (Peabody and others, 2004; Veloski and others, 2005). Additionally, vignettes have been combined with Delphi methodology to achieve expert consensus in optimizing treatment, as well as in establishing evidence gaps (Rose and Kagan, 1998). Use of open, rather than closed, questions in vignettes has been reported to better describe clinicians’ actual practice patterns (Pham and others, 2009) and provide insight into what is accepted current practice.

The aim of this study was to survey veterinarians about the current management of KCS and acute glaucoma. Additionally, we aimed to explore the variation in treatment amongst all veterinarians and between general practitioners and veterinarians with postgraduate training in ophthalmology.

**Materials and methods**

**Sampling and data collection**

The target population was all members of the veterinary profession in the UK. The sampling frames were a convenience sample of veterinarians on a mailing list held by the Centre for Evidence-based Veterinary Medicine (CEVM) (identified from another survey initially approaching respondents using a list of RCVS members who were willing to be contacted, Nielsen and others, 2014), and attendees at the British Association of Veterinary Ophthalmologists (BrAVO) Winter conference (2011).

A questionnaire (Appendix 1) was constructed consisting of 22 open and closed-end questions across five sections as part of a student research project (Corinne Wigfall). These sections covered the diagnostic tools used for ophthalmological cases, the sources of information accessed by vets and factors considered in clinical decision-making for ocular conditions, as well as questions relating to respondent demographics (age, gender, year of graduation, ophthalmology postgraduate certification or training). The additional two sections presented two clinical vignettes—the first based on a West Highland White Terrier with KCS and the second a Cocker Spaniel presenting with acute PACG. After each vignette, veterinarians were asked what treatments, additional investigations, long term management and recheck advice they would give for each case. The design
of the vignettes was based on “textbook” cases to minimize diagnostic confusion while the
associated questions were derived from a similar survey undertaken by Davies (2015). The
questionnaire was pre-tested by 20 people, and piloted by eight veterinarians and three non-
clinicians.

An online questionnaire was constructed and administered through cloud-based software
(SurveyMonkey Inc., California, USA) to the CEVM mailing list. Online respondents were
encouraged to fill out the questionnaire by being entered into a prize draw for a £50 gift;
respondents were anonymized for analysis. The online survey was initiated October 26, 2011 and
closed November 18, 2011. A first reminder was sent 2 weeks after the initial email followed by a
final reminder two days before survey close. Paper questionnaires identical in sequence and content
to the online questionnaire were distributed to the attendees during one day of the British
Association of Veterinary Ophthalmologists Winter conference and were collected back by three of
the authors at the end of the day (November 5, 2011).

Ethical approval for the study was received from the ethics committee at the School of Veterinary
Medicine and Science at The University of Nottingham.

Data management and analysis
Returned online responses were downloaded to Microsoft Excel V.14.0.6 (2010 Microsoft
Corporation) whilst paper questionnaire responses were manually entered into the same
spreadsheet. Data relating to proposed treatments and diagnostic investigations were extracted
from open ended responses by one coder (Constance White) and categorically classified into generic
drug name and/or category, surgical or procedural interventions, diagnostic test, and other patient
assessments. Data relating to long term recommendations were extracted by one coder (Constance
White) and classified into categories relating to prognosis, salvage treatment options, chronicity, and
owner communication/compliance. Suggested reevaluation times were converted from text to
numerals and where ranges were given, mean time calculated.

Statistical analysis was performed with a commercially available statistical package (Stata IC13).
Continuous data (age, years since graduation, recheck intervals) were assessed for normality by the
Shapiro-Wilk normality test and were subsequently analyzed using Mann-Whitney U tests. Chi-
square tests were used to compare categorical data between groups except when expected cell
counts were ≤ 5, where the more conservative Fisher’s exact test was used. Not all respondents
answered all questions; proportions are calculated using the total numbers of respondents
completing each question unless otherwise indicated. Statistical significance was set at the 0.05
level; when multiple comparisons were undertaken, p values were adjusted for significance at this
level with the Dunn-Bonferroni method (Pagano and others, 2009). In brief, for a p value to reach
significance with correction for multiple comparisons, value must be <0.05/k where k is the number
of comparisons. Significant p values are reported in text when not included in tables.

Results
Response rate

Of 1421 successful email invitations, 490 (34.5%) online questionnaires were returned. Of those, 392 were from veterinarians engaged in small animal practice. Sixty one paper questionnaires were returned by British Veterinary Ophthalmologist Association (BrAVO) conference attendees (total number of conference attendees unknown). Of the total number of eligible responses (453), 70 were engaged in or training for postgraduate ophthalmology practice; from here on known as ‘PGs’ while 383 were engaged in general practice (from here on known as ‘GPs’). Not all 453 respondents answered all questions within the questionnaire (Table 1).

Table 1 Demographic and vignette question response rate. KCS = Keratoconjunctivitis sicca

<table>
<thead>
<tr>
<th>Overall n</th>
<th>Overall %</th>
<th>GP n</th>
<th>GP %</th>
<th>PG n</th>
<th>PG %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survey</td>
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<td>100</td>
<td>383</td>
<td>100</td>
<td>70</td>
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<tr>
<td>Age</td>
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<td>72.8</td>
<td>260</td>
<td>67.9</td>
<td>70</td>
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<tr>
<td>Gender</td>
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<td>73.3</td>
<td>262</td>
<td>68.4</td>
<td>70</td>
</tr>
<tr>
<td>Graduation year</td>
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<td>73.1</td>
<td>261</td>
<td>68.1</td>
<td>70</td>
</tr>
<tr>
<td>KCS treatment</td>
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<td>88.1</td>
<td>329</td>
<td>85.9</td>
<td>70</td>
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<tr>
<td>Further investigation KCS</td>
<td>395</td>
<td>87.2</td>
<td>195</td>
<td>50.9</td>
<td>53</td>
</tr>
<tr>
<td>KCS diagnostics</td>
<td>252</td>
<td>55.6</td>
<td>197</td>
<td>51.4</td>
<td>55</td>
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<tr>
<td>KCS recheck interval</td>
<td>396</td>
<td>87.4</td>
<td>326</td>
<td>85.1</td>
<td>70</td>
</tr>
<tr>
<td>KCS long term management</td>
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<td>73.7</td>
<td>266</td>
<td>69.5</td>
<td>68</td>
</tr>
<tr>
<td>Glaucoma treatment</td>
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<td>72.8</td>
<td>260</td>
<td>67.9</td>
<td>70</td>
</tr>
<tr>
<td>Glaucoma further investigation</td>
<td>323</td>
<td>71.3</td>
<td>254</td>
<td>66.3</td>
<td>69</td>
</tr>
<tr>
<td>Glaucoma diagnostics</td>
<td>260</td>
<td>57.4</td>
<td>191</td>
<td>50.0</td>
<td>69</td>
</tr>
<tr>
<td>Glaucoma recheck interval</td>
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<td>57.2</td>
<td>206</td>
<td>53.8</td>
<td>53</td>
</tr>
<tr>
<td>Glaucoma long term management</td>
<td>262</td>
<td>57.8</td>
<td>194</td>
<td>50.6</td>
<td>68</td>
</tr>
</tbody>
</table>

Respondent characteristics

Sixty three percent of all respondents were female, with a somewhat higher proportion of males in the PG group, a difference which did not reach statistical significance. Overall median age of respondents was 37 years, with PGs significantly older than the GP group. Median year of qualification was significantly earlier for PGs than for GPs. Analysis stratified by gender did not eliminate age or year of qualification differences between PGs and GPs (Table 2). When participants were de-anonymized by email address subsequent to analysis, credentials and practice type could be ascertained for 41 of the 70 PG respondents. Of those, eight were RCVS Specialists in ophthalmology, 28 were designated ophthalmology certificate holders (26/28 CertVOphthal), four were ophthalmology certificate candidates, and one was a non-identified certificate candidate.

Overall, 88% (36/41) of those successfully de-anonymized were in referral practice at the time of the survey.

Table 2 Participant responses to demographic questions, comparison between practitioner groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Overall n</th>
<th>Overall %</th>
<th>GP n</th>
<th>GP</th>
<th>PG n</th>
<th>PG</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>123</td>
<td>37.0%</td>
<td>91</td>
<td>34.7%</td>
<td>32</td>
<td>45.7%</td>
<td>0.091</td>
</tr>
<tr>
<td>Female</td>
<td>209</td>
<td>63.0%</td>
<td>171</td>
<td>65.3%</td>
<td>38</td>
<td>54.3%</td>
<td></td>
</tr>
<tr>
<td>No answer given</td>
<td>121</td>
<td>121</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Age

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Range</th>
<th>Median Age (all)</th>
<th>Median Age (male)</th>
<th>Median Age (female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>260</td>
<td>35.5</td>
<td>9.5</td>
<td>37.0</td>
<td>40.0</td>
<td>33.0</td>
</tr>
<tr>
<td>No answer given</td>
<td>123</td>
<td>32</td>
<td></td>
<td></td>
<td>32</td>
<td>38</td>
</tr>
</tbody>
</table>

### Year of qualification

<table>
<thead>
<tr>
<th>Year of Qualification</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Range</th>
<th>Median Year Qualified (all)</th>
<th>Median Year Qualified (male)</th>
<th>Median Year Qualified (female)</th>
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<tr>
<td>No answer given</td>
<td>122</td>
<td>122</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Categorical data chi square test. Continuous data Mann-Whitney test

*Significant with Bonferroni corrected p <0.05

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**Keratoconjunctivitis sicca**

Initial KCS treatment recommendations were offered by 399 respondents. Six different topical treatments were nominated (Table 3). The majority of both groups recommended cyclosporine (CSA) and an ocular lubricant. However, a significantly larger portion of GPs suggested using topical antibiotics.

Most respondents suggested a combination of topical therapies; a wider range of combinations were offered by GPs (GPs 12 combinations, PGs 8 combinations). A majority (98%) of respondents suggested one of eight different combinations of the four most common topicals (Figure 1). The top four combinations were recommended by 85.1% of GPs and 90.0% of PGs. PGs were significantly more likely to use topical CSA in combination with lubricant as sole treatment (chi square p=0.001) but no other significant differences were found. Amongst both groups, there were few recommendations of systemic therapies: 34 veterinarians recommended a systemic nonsteroidal anti-inflammatory (NSAID), eight veterinarians recommended systemic antibiotics, and one recommended systemic steroids for initial treatment.

Of 395 veterinarians who considered whether further investigation of KCS was warranted, a majority (63.8%) recommended further diagnostic tests (Figure 2). The most common suggestion was fluorescein staining. PGs were significantly more likely to recommend culture, tear film breakup testing, slit lamp evaluation, and Rose Bengal staining when compared to GPs (p<0.003 for each item, Fisher’s exact test). Small numbers of respondents (<12 per recommendation) suggested evaluation for drug history, atopic dermatitis, and neurogenic causes of dry eye. Suggested recheck intervals differed significantly between GPs and PGs. Median time suggested for first recheck was 7 days (range 2-52, IQR 7-14 days) for GPs versus a median of 14 days (range 5-60, IQR 12-28 days) for PGs (Mann Whitney U p=0.0000).

More than 40% of both groups discussed the need for long term therapy and regular assessment.

Although the questionnaire did not solicit recommendations for refractory disease, multiple respondents offered suggestions in case of treatment failure: twelve individuals recommended compounded cyclosporine ophthalmic suspension while six suggested tacrolimus. Parotid duct transposition was considered by ten respondents in each group.
Table 3 Topical treatment recommendations for KCS by participants. NSAID = Nonsteroidal anti-inflammatory drug

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Overall n</th>
<th>Overall %</th>
<th>GP n</th>
<th>GP %</th>
<th>PG n</th>
<th>PG %</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine</td>
<td>371</td>
<td>93.0</td>
<td>304</td>
<td>92.4</td>
<td>67</td>
<td>95.7</td>
<td>0.324</td>
</tr>
<tr>
<td>Lubricant or tear replacement</td>
<td>319</td>
<td>78.0</td>
<td>256</td>
<td>77.8</td>
<td>63</td>
<td>90.0</td>
<td>0.021</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>277</td>
<td>69.4</td>
<td>239</td>
<td>72.6</td>
<td>38</td>
<td>54.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Steroid</td>
<td>58</td>
<td>14.5</td>
<td>44</td>
<td>13.4</td>
<td>14</td>
<td>20.0</td>
<td>0.153</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>2</td>
<td>0.5</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>2.9</td>
<td>0.030</td>
</tr>
<tr>
<td>Topical NSAID</td>
<td>1</td>
<td>0.25</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>1.4</td>
<td>0.175</td>
</tr>
</tbody>
</table>

*Significant with Bonferroni corrected p <0.05, chi square test unless otherwise indicated

† Fisher’s exact test

Acute Glaucoma

A total of 330 veterinarians made treatment recommendations for PACG. Half of all GPs indicated a desire to refer the glaucoma patient acutely but many of those also suggested some initial treatments. Ten topical agents for PACG management were nominated (Table 4). Of those, PGs were significantly more likely to recommend a prostaglandin analogue (PGA) and steroid. GPs suggested the use of pilocarpine significantly more often than PGs. Respondents who suggested pilocarpine were not significantly different in age (Mann Whitney U p=0.5989), years of qualification (Mann Whitney U p=0.8615), or gender from other veterinarians (chi square p=0.428). There were small but significant differences in choice of CAI and PGA agents selected, with a greater fraction of PGs suggesting brinzolamide and travoprost.

Nineteen combinations of the five most commonly suggested topicals were recommended by respondents (GPs 18 combinations, PGs 10 combinations). The ten most common combinations were suggested by 72.6% of GPs and 95.7% of PGs (Figure 3). The top four combinations were recommended by 55.3% of GPs and 77.2% of PGs. More than half (52.9%) of PGs chose a PGA (typically latanoprost or travoprost) in combination with a carbonic anhydrase inhibitor (CAI; predominate dorzolamide), with or without additional timolol and/or topical steroid. GPs nominated PGAs significantly less often and were more likely to suggest a CAI alone or in combination with topicals other than PGAs. Fewer GPs suggested CAI in fixed combination with timolol (GPs 15 of 148 CAI suggestions, PGs 13 of 50 CAI suggestions, chi square p=0.001).

Many systemic therapies were also recommended (Table 5). Analgesic or anti-inflammatory drugs were suggested by a large proportion, with NSAIDs most frequently specified. Twenty individuals used a combination of products. Small numbers of respondents recommended systemic mannitol or CAI to reduce intraocular pressure (IOP). A handful of respondents recommended antihypertensive or diuretic drugs. No significant differences were found between GPs and PGs in their recommendations for systemic agents.

Of the 260 respondents who answered questions about further investigations, the majority (79.0%) recommended further diagnostics but few GPs made specific diagnostic recommendations (Figure
4). PGs suggested gonioscopy, slit lamp evaluation, ocular ultrasound, and Schirmer tear testing at significantly greater rates than GPs (chi square p<0.001 for each test). After adjustment for access to a gonioscopy lens, PGs were still significantly more likely to recommend gonioscopy (chi square p=0.000). Specific assessment for uveitis (n=7), lens luxation (n=27), and vision (n=7) were recommended by a minority of each group. A significantly higher proportion of PGs recommended evaluation of the contralateral eye (3.1% GPs, 27.5% PGs, chi square p=0.000).

Suggested recheck intervals did not significantly differ between GPs and PGs. Median time suggested for first recheck was 1.5 days (range 1-14, IQR 1-3 days) for GPs versus a median of 2 days (range 0.6-7, IQR 1-3.5 days) for PGs. More than a third of PGs (n=25) recommended hospitalization until IOP normalized, a significantly greater proportion than GPs (n=12, chi square p<0.001).

Of the 262 respondents who gave long term management recommendations, PGs and GPs were equally likely to discuss the need for ongoing treatment of glaucoma (11.9% GPs, 17.9% PGs), regular monitoring (30.4 % GPs, 36.2% PGs), and long term prognosis (13.4% GPs, 20.3% PGs). More than half of PGs (56.5%) discussed evaluation, prognosis and/or prophylaxis of the contralateral eye, whilst significantly fewer GPs (23.7%) did so (chi square p=0.000).

Table 4 Topical treatment recommendations for acute glaucoma by participants. NSAID =

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Overall n</th>
<th>Overall %</th>
<th>GP n</th>
<th>GP %</th>
<th>PG n</th>
<th>PG %</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonic anhydrase inhibitor</td>
<td>198</td>
<td>60.0</td>
<td>148</td>
<td>56.9</td>
<td>50</td>
<td>71.4</td>
<td>0.028</td>
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<td>Dorzolamide</td>
<td>151</td>
<td>45.8</td>
<td>123</td>
<td>47.3</td>
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<td>Brinzolamide</td>
<td>31</td>
<td>9.4</td>
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<td>5.8</td>
<td>16</td>
<td>22.9</td>
<td>*0.000</td>
</tr>
<tr>
<td>Either</td>
<td>11</td>
<td>3.3</td>
<td>7</td>
<td>2.7</td>
<td>4</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
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<td>1.5</td>
<td>3</td>
<td>1.2</td>
<td>2</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>Prostaglandin analogue</td>
<td>128</td>
<td>38.8</td>
<td>72</td>
<td>27.7</td>
<td>56</td>
<td>80.0</td>
<td>*0.000</td>
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<td>Latanoprost</td>
<td>81</td>
<td>24.5</td>
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<td>20.4</td>
<td>28</td>
<td>40.0</td>
<td>*0.001</td>
</tr>
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</tr>
<tr>
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<td>1.9</td>
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<td>2.9</td>
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<td>20.0</td>
<td>0.030</td>
</tr>
<tr>
<td>Steroid</td>
<td>30</td>
<td>9.1</td>
<td>16</td>
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<td>14</td>
<td>20.0</td>
<td>*0.000</td>
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<td>Pilocarpine</td>
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<td>0</td>
<td>*0.003</td>
</tr>
<tr>
<td>Atropine</td>
<td>13</td>
<td>4.0</td>
<td>13</td>
<td>5.0</td>
<td>0</td>
<td>0</td>
<td>±0.078</td>
</tr>
<tr>
<td>NSAID (topical)</td>
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<td>12</td>
<td>4.6</td>
<td>0</td>
<td>0</td>
<td>±0.078</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>10</td>
<td>3.0</td>
<td>9</td>
<td>3.5</td>
<td>1</td>
<td>1.4</td>
<td>±0.695</td>
</tr>
<tr>
<td>Lubricant</td>
<td>6</td>
<td>1.8</td>
<td>5</td>
<td>1.9</td>
<td>1</td>
<td>1.4</td>
<td>±0.100</td>
</tr>
<tr>
<td>Iopidine</td>
<td>1</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.4</td>
<td>±0.212</td>
</tr>
</tbody>
</table>

*Significant with Bonferroni corrected p <0.05, chi square test unless otherwise indicated

† Fisher’s exact test
Table 5. Systemic glaucoma therapies suggested by participants. NSAID = Nonsteroidal anti-inflammatory drug; IOP = Intraocular pressure; IV = Intravenous; CAI = Carbonic Anhydrase Inhibitor; ACE = Angiotensin Converting Enzyme.

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Overall n</th>
<th>Overall %</th>
<th>GP n</th>
<th>GP %</th>
<th>PG n</th>
<th>PG %</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain/antiinflammatory</td>
<td>183</td>
<td>55.5</td>
<td>144</td>
<td>55.3</td>
<td>39</td>
<td>55.7</td>
<td>0.961</td>
</tr>
<tr>
<td>NSAID</td>
<td>155</td>
<td>47.0</td>
<td>118</td>
<td>45.4</td>
<td>37</td>
<td>52.9</td>
<td>0.266</td>
</tr>
<tr>
<td>Unspecified analgesia</td>
<td>25</td>
<td>7.6</td>
<td>24</td>
<td>9.2</td>
<td>1</td>
<td>1.4</td>
<td>ǂ0.038</td>
</tr>
<tr>
<td>Opioid or tramadol</td>
<td>19</td>
<td>5.8</td>
<td>10</td>
<td>3.8</td>
<td>9</td>
<td>12.9</td>
<td>*0.004</td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>4</td>
<td>1.2</td>
<td>3</td>
<td>1.2</td>
<td>1</td>
<td>1.4</td>
<td>ǂ1.000</td>
</tr>
<tr>
<td>All pain/antiinflammatory</td>
<td>183</td>
<td>55.5</td>
<td>144</td>
<td>55.3</td>
<td>39</td>
<td>55.7</td>
<td>0.961</td>
</tr>
<tr>
<td>IOP agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV mannitol</td>
<td>34</td>
<td>10.3</td>
<td>26</td>
<td>10.0</td>
<td>8</td>
<td>11.4</td>
<td>0.727</td>
</tr>
<tr>
<td>Oral CAI</td>
<td>17</td>
<td>5.2</td>
<td>16</td>
<td>6.2</td>
<td>1</td>
<td>1.4</td>
<td>ǂ0.137</td>
</tr>
<tr>
<td>Hypotensives/diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2</td>
<td>0.6</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>2.9</td>
<td>ǂ0.044</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>1</td>
<td>0.3</td>
<td>1</td>
<td>0.4</td>
<td>0</td>
<td>0.0</td>
<td>ǂ1.000</td>
</tr>
<tr>
<td>Furosemide</td>
<td>4</td>
<td>1.2</td>
<td>4</td>
<td>1.5</td>
<td>0</td>
<td>0.0</td>
<td>ǂ0.582</td>
</tr>
<tr>
<td>Referral</td>
<td>133</td>
<td>40.3</td>
<td>130</td>
<td>50.0</td>
<td>3</td>
<td>4.3</td>
<td>*0.000</td>
</tr>
</tbody>
</table>

*Significant with Bonferroni corrected p<0.05, chi square test unless otherwise indicated
ǂ Fisher’s exact test

Discussion

Prior work has established that substantial treatment variation may occur in the management of canine diabetes and heart failure (Davies and others, 2015; Sinclair and others, 2014). This study demonstrates similar variation, particularly in the treatment of PACG. We speculate that this variation may be driven by knowledge gaps influenced by one or more of the following factors: lack of evidence-based and/or consensus guidelines, access to information, or differences in caseload and/or practice setting.

For KCS, fairly robust evidence (grade I, Roudebush and others, 2004) exists for topical CSA efficacy in prospective clinical trials and an approved veterinary ophthalmic preparation has been available for more than two decades (Kaswan and others, 1989; Morgan and Abrams, 1991; Olivero and others, 1991; Sansom and others, 1995). Frequent nomination of CSA for KCS treatment likely reflects acceptance of efficacy and incorporation into standards of care. The preference for CSA over tacrolimus may be driven by CSA’s availability as a licensed veterinary product as well as current evidence which suggests equal efficacy of CSA and tacrolimus for treatment-naïve KCS (Berdoulay and others, 2005, Hendrix and others, 2011). Similarly, there was general agreement in favour of topical lubricant. Prior to the introduction of CSA, lubricants were the mainstay of KCS medical therapy (Blogg, 1980) and, extrapolating from human dry eye, may be reasonably expected to provide some symptomatic relief and corneal protection (Alves and others, 2013).

Apart from CSA, most topicals used in KCS have limited published evidence for efficacy and this may account for wider variation in their recommended use. There is sparse data regarding the...
prevalence of secondary infection with conflicting recommendations for antibiotic use in KCS (Giuliano and Moore, 2007; Maggs and others, 2012; Martin, 2010; Petersen-Jones, 1997; Salisbury and others, 1995). Topical steroids are suggested by some veterinary ophthalmologists to decrease conjunctival inflammation, discomfort and corneal scarring in KCS (Giuliano and Moore, 2007).

Topical steroid recommendations appear to rely on clinician experience and possibly extrapolation from the human literature which has shown benefit in dry eye (Messmer, 2015). While broad general agreement was found for KCS management, treatment suggestions for PACG were more varied. GPs nominated topical PGAs significantly less frequently than did PGs while use of CAIs was more similar between the two groups. There is reasonable evidence (grade III, Roudesh and others, 2004) for both PGA and CAI efficacy for IOP reduction in beagles with open-angle glaucoma, with PGAs offering superior duration and magnitude of IOP reduction (Gelatt and McKay, 2001a, 2001b, 2002, 2004b; Plummer and others, 2006). However, no clinical trials assessing safety or efficacy of these agents alone or in combination have been reported for the more common syndrome of PACG (reviewed by Maślanka, 2015a, 2015b). Topical PGAs are preferred over systemic agents in achieving IOP reduction by some authors (Alario and others, 2015; Maślanka, 2015b), a view that was paralleled by our results. Clinical uncertainty in recognizing PGA contraindications (anterior lens luxation and uveitis) may account for the lower rate of GP recommendation. However, other factors may play a role in differential recommendations: pilocarpine has similar contraindications yet was recommended by a number of GPs. It is striking that no PG recommended pilocarpine; veterinary ophthalmologists appear to discourage pilocarpine due to ocular irritation and perceived superiority of other ocular hypotensives (Alario and others, 2015). Choice of topical PGA and CAI also varied between GP and PG groups with the latter group nominating travoprost and brinzolamide significantly more frequently. Reasons for product choice were not elicited in our questionnaire and we are unaware of any comparative efficacy trials between dorzolamide and brinzolamide, or between latanoprost and travoprost, in acute canine glaucoma; however, brinzolamide is suggested to result in less ocular irritation relative to dorzolamide (Alario and others, 2015). Likewise, more PGs recommended a topical steroid. Although we did not elicit the clinical reasoning behind treatment suggestions, steroids may have been recommended due to the putative role of inflammation in both genesis and progression of PACG (Dees and others, 2014; Reilly and others, 2005); steroids may exacerbate ocular hypertension in cats and dogs but the response may vary by individual and with the concurrent use of PGA (Herring, Herring, and Ward, 2004; Gelatt and McKay, 1998; Gosling and others, 2016; Kahane and others, 2016). However, we are unaware of any studies assessing the use of steroids in PACG (apart from prophylaxis in unaffected but at-risk eyes). As would be anticipated, PGs recommended a greater number of specific ophthalmic diagnostics.

GP suggestions for additional investigation generally agreed with PG recommendations when the suggested test was inexpensive and did not require specialized equipment or expertise. In particular, gonioscopy may be difficult to master without routine practice and we are not aware of any readily available training resources for GPs.

Recheck intervals and judgement regarding natural history and prognosis of KCS and glaucoma were generally concordant between both groups with one exception: recheck intervals for KCS were significantly shorter for GPs than for PGs. Topical CSA typically lags 3-4 weeks for maximal increase in tear production (Olivero and others, 1991, Samson and others, 1995). The shorter median interval suggested by GPs may reflect severity differences in initial presentation, misunderstanding
of CSA pharmacodynamics, decreased clinical confidence, or a variety of other factors not captured in this survey. Alternatively, GP versus PG clinic proximity may affect recheck intervals amenable to clients; however, the similarity of suggested glaucoma recheck intervals between the two groups argues against client convenience as a driving factor.

Veterinarians in primary practice are required to have proficiency in multiple domains and may have limited access to literature unless affiliated with academic practice; availability of veterinary ophthalmologist advice may also vary due to geographic, social network, and practice characteristics. Although management guides used by GPs uniformly recommend CSA and provide algorithms for the treatment of KCS, most PACG references are less directive in treatment recommendations and typically provide a more general pharmacologic review, with referral often recommended as the preferred treatment strategy (Clode, 2015; Colitz, 2010; Feinstein and others, 2009). We speculate that the wider range of recommendations for PACG encountered amongst our GP respondents may reflect a lack of clear and concise treatment guidelines for this condition; guidance which may be particularly needed for cases which cannot be referred. PGs in this survey also varied in their treatment recommendations, particularly with respect to the use of combinations of topical agents; variable use of steroids and antibiotics in the case of KCS, as well as agents combined with PGAs in PACG, suggest treatment uncertainties which may need additional data to resolve. We suggest that establishing current practice in treating companion animal ocular disease may at least allow for benchmarking of individual practitioners against their colleagues. Additionally, these surveys can both highlight clinical questions of high priority and identify areas needful of consensus guidance when evidence is lacking. We suggest incorporation of Delphi or similar anonymized methods in formulating veterinary ophthalmology guidelines (Jones and Hunter, 1995). Adherence, credibility, and feasibility of consensus guidelines is suggested to improve when general practitioners are included on consensus panels (Allan et al., 2015; Carlsen, Glen ton, and Pope, 2007; Carlsen and Norheim, 2008; Rashidian, Eccles, and Russell, 2008). Assemblage of electronic cohort data from both referral and first opinion practices, as well as consideration of multi-centre pragmatic clinical trials, may be cost-effective paths to generating better and externally valid evidence.

Study limitations
This survey was distributed to a subset of RCVS registered veterinarians who had expressed willingness to be contacted by the CEVM, as well as to attendees at an ophthalmology meeting. Additionally, although the majority of respondents completed the survey via a web-based instrument, questionnaire format (paper versus web-based) may have resulted in qualitative or quantitative differences in responses. Several levels of self-selection bias may have been introduced: veterinarians who were willing to be contacted may have a greater interest in evidence-based medicine while veterinarians who responded to the web-based survey may have better access or understanding of a web-based instruments. Respondents were more likely to be female and newer graduates than RCVS members in total; a contemporary survey of RCVS members found a median qualification year of 1991, with approximate gender parity in registered members (Robertson-Smith and others, 2010). As with any vignette-based survey, conformity of recommendations to actual practice cannot be established.

Conclusion
This survey of veterinarians in the United Kingdom found variation in the treatment of KCS and PACG between practitioners. Variation in management may be driven by a limited evidence base, lack of clinical guidelines, heterogeneous training and practice settings, and clinical confidence or interest on the part of respondents. Additionally, greater treatment variation was found in management of PACG, a condition for which no approved veterinary products are available. Further work is needed in assessing factors responsible for treatment variation and in optimizing resources and strategies for building and disseminating evidence-graded, relevant diagnostic and treatment recommendations to practitioners.

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References


Eight most common recommended topical treatment combinations for KCS (numbers indicate number of respondents nominating that combination, percentage of total respondents recommending KCS treatments was 330 GPs, 70 PGs)
Additional diagnostic tests recommended by those who suggested further evaluation for KCS (numbers indicate number of respondents nominating that diagnostic test, percentage of total respondents recommending KCS diagnostics was 197 GPs, 55 PGs)
Figure 3

Most common recommended topical treatment combinations for glaucoma (CAI = topical carbonic anhydrase inhibitor; PGA = prostaglandin analog, (numbers indicate number of respondents recommending that glaucoma treatment, percentage of total respondents recommending KCS diagnostics was 260 GPs, 70 PGs)

- CAI/pilocarpine: 10 GPs, 13 PGs
- Timolol only: 9 GPs, 5 PGs
- CAI/timolol: 10 GPs, 6 PGs
- Pilocarpine only: 13 GPs, 0 PGs
- CAI/PGA/steroid: 5 GPs, 6 PGs
- PGA/steroid: 6 GPs, 1 PGs
- PGA/CAI/timolol: 10 GPs, 4 PGs
- PGA only: 27 GPs, 13 PGs
- CAI/PGA: 31 GPs, 20 PGs
- CAI only: 82 GPs, 11 PGs
Figure 4

Additional diagnostic tests recommended by those who suggested further evaluation for glaucoma (numbers indicate number of respondents nominating that diagnostic test, percentage of total respondents recommending glaucoma diagnostics was 191 GPs, 69 PGs)

- **Electroretinography**: 1 GPs, 0 PGs
- **Schirmer tear test**: 1 GPs, 5 PGs
- **Blood pressure**: 9 GPs, 0 PGs
- **Laboratory investigation**: 14 GPs, 3 PGs
- **Fluorescein stain**: 12 GPs, 4 PGs
- **Slit lamp exam**: 11 GPs, 11 PGs
- **Ultrasound**: 20 GPs, 19 PGs
- **Gonioscopy**: 19 GPs, 62 PGs