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# Determining resolution of *Angiostrongylus vasorum* in dogs following anthelmintic treatment with an imidacloprid 10 per cent/moxidectin 2.5 per cent spot-on

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## ABSTRACT

**Objectives** To determine the time from treatment with a product containing imidacloprid 10 per cent/moxidectin 2.5 per cent spot-on (Advocate™), to dogs becoming negative for *Angiostrongylus vasorum (A. vasorum)*. The authors hypothesised that most dogs would have resolution of *A. vasorum* within four weeks of treatment with Advocate™.

**Design** Prospective, non-randomised, prepost treatment study.

**Setting** Cases were enrolled from general practices along the southern coast of the United Kingdom.

**Participants** Nine dogs completed the study and were enrolled if *A. vasorum* had been diagnosed based on a positive commercially available, in-clinic, serological *A. vasorum* antigen test (Angio Detect®) or Baermann performed at an external laboratory or both.

**Interventions** The only treatment *A. vasorum*-positive dogs received was Advocate™ which was applied at the time of diagnosis and reapplied if necessary at four-weekly intervals until dogs tested negative by Angio Detect.

**Primary outcome measures** Angio Detect® was performed and Advocate™ was reapplied at four-weekly intervals until dogs tested negative by this method.

**Secondary outcome measures** Baermann was also performed at four-weekly intervals until dogs tested negative by this method.

**Results** Application of Advocate™ was an effective treatment for *A. vasorum* infection in dogs and resulted in resolution of the infection, based on Angio Detect® testing and Baermann, within four weeks, in eight out of nine dogs. Post-treatment Angio Detect® testing was concordant with Baermann in seven of nine dogs.

**Conclusions** Application of Advocate™ was an effective treatment for *A. vasorum* infection in dogs and resulted in resolution of the infection within four weeks in most dogs. Repeat Angio Detect® testing is recommended following treatment of *A. vasorum* to confirm resolution of the infection.

## INTRODUCTION

*Angiostrongylus vasorum* (*A. vasorum*) is a nematode parasite with a diffuse distribution across the United Kingdom (UK) in addition to mainland Europe, Asia and Africa, as well as an endemic focus in Newfoundland, Canada.[1] Appropriate diagnosis and treatment is generally associated with a good prognosis for recovery[1] in dogs with *A. vasorum* infection; however, the disease can be fatal if left untreated. Mature parasites inhabit the right heart, pulmonary artery and pulmonary arterioles. The host's inflammatory response against these parasites results in respiratory disease; however, *A. vasorum* can also cause haemostatic disorders[1] and concern for infection sometimes becomes apparent if prolonged haemorrhage is detected at the time of surgery.

The underlying cause of bleeding is poorly understood but may be related to a consumptive coagulopathy.[1 2] Traditional coagulation parameters, such as activated partial thromboplastin time (aPTT) and partial prothrombin time (PT), can remain within normal limits in many infected dogs,[2] and a previous study found that thrombocytopenia was only present in 4.2 per cent of infected dogs at the time of diagnosis.[3]

Thromboelastography (TEG) is a haemostatic assay that measures the global properties of whole blood clot formation; in one study, 17 out of 18 *A. vasorum*-infected dogs presenting to a referral centre with signs of bleeding on physical examination had evidence of hypocoagulability on TEG.[2] TEG samples must be processed within a few minutes of venepuncture, making this unavailable to the large majority of primary care veterinary practices.

If only traditional coagulation parameters and a complete blood count are assessed before surgery, dogs with haemostatic disorders secondary to *A. vasorum* may be overlooked. A decision as to when to pursue elective surgery following treatment of *A. vasorum* therefore has

to be based on the results of other diagnostic tests, such as Baermann or serological testing.

The aims of this study were to determine the time from treatment with an imidacloprid 10 per cent/moxidectin 2.5 per cent spot-on (Advocate™ spot-on solution, Bayer, Reading, Berkshire) to dogs becoming negative for *A. vasorum* and to investigate whether there were any discrepancies between post-treatment Baermann and a commercially available, in-house, serological *A. vasorum* antigen test (Angio Detect® test, IDEXX Laboratories, Westbrook, Maine, USA) for detection of persistent infection following treatment.

Correctly determining when the infection has resolved will have important implications for practitioners including when to transition from therapeutic to preventative treatment and when to perform elective surgeries.

## METHODS

Dogs were recruited from primary care veterinary practices and were not referred. Clinical history, including signalment and presenting clinical signs, were obtained if available. A diagnosis of *A. vasorum* was obtained by means of either a positive Angio Detect® test or Baermann performed at an external laboratory, or both. The only treatment *A. vasorum*-positive dogs received was Advocate™ spot-on solution. Angio Detect® test was performed and Advocate™ was reapplied at four-weekly intervals until dogs tested negative by this method. Baermann was performed on a single faecal sample at four-weekly intervals until dogs tested negative by this method.

## RESULTS

Nine dogs were diagnosed with *A. vasorum* between December 2013 and July 2015. Where recorded, breeds affected included Staffordshire bull terrier (1), lurcher (1), labrador retriever (1), English springer spaniel (1), bulldog (1), Manchester terrier (1) and crossbreed (1). The median age of dogs included in the study was 6 years 6 months (range 9 months to 10 years 7 months). Presenting clinical signs and clinicopathological findings were available for seven dogs. Two of seven dogs were asymptomatic and routine testing was performed before elective surgical procedures. Five dogs presented with clinicopathological abnormalities, including gingival haemorrhage (1), prolonged PT (1), prolonged aPTT (1), low fibrinogen (1), haematochezia (1), regenerative anaemia (1) and coughing (2) (see Table 1).

A diagnosis of *A. vasorum* was based on positive Angio Detect® in eight dogs and Baermann in two dogs. Dog number 8 had an Angio Detect® and Baermann performed at the time of presentation; the latter was found to be negative at the time of diagnosis (see table 1).

Four weeks following diagnosis and first application of Advocate™, all nine dogs were negative on Baermann, eight dogs were negative on Angio Detect® testing and

**TABLE 1:** Results

| Number | Breed | Age | Sex | Clinical signs and laboratory findings | Initial diagnostic method | AD at 4 weeks | B at 4 weeks | AD at 8 weeks | B at 8 weeks | AD at 12 weeks | B at 12 weeks |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Lurcher | 6 years | FN | Gingival haemorrhage, prolonged aPTT and PT, decreased fibrinogen | AD | Negative | Negative | NP | NP | NP | NP |
| 2 | Labrador retriever | 8 years | MN | Acute haemorrhagic diarrhoea | B | Negative | Negative | NP | NP | NP | NP |
| 3 | Unknown | Unknown | Unknown | None | AD | Positive | Negative | Positive | NP | Negative | NP |
| 4 | English springer spaniel | 9 years 7 months | ME | Regenerative anaemia (PCV 18%), thrombocytopenia, haematochezia | AD | Negative | Negative | NP | NP | NP | NP |
| 5 | Staffordshire bull terrier | 9 years | FN | Intermittent cough for two months | AD | Negative | Negative | NP | NP | NP | NP |
| 6 | Unknown | Unknown | Unknown | Unknown | AD | Negative | Negative | NP | NP | NP | NP |
| 7 | Bulldog | 2 years 10 months | FE | None | AD | Negative | Negative | NP | NP | NP | NP |
| 8 | Manchester terrier | 10 years 7 months | MN | Coughing | AD; B (negative) | Negative | Negative | NP | NP | NP | NP |
| 9 | Crossbreed | 9 months | MN | None | AD | Negative | Negative | NP | NP | NP | NP |

AD, Angio Detect test; aPTT, activated partial thromboplastin time; B, Baermann; FE, female entire; FN,female neutered ME, male entire; MN, male neutered; NP, test not performed; PCV, packed cell volume; PT, prothrombin time.

one dog was positive (dog number 3). This dog received a repeat application of Advocate™ four weeks postdiagnosis. The dog remained Angio Detect® -positive at 8 weeks (Baermann was not repeated) and received a third application of Advocate™; Angio Detect® test repeated at 12 weeks postdiagnosis was negative.

## DISCUSSION

Dog 8 with discrepant Angio Detect® and Baermann results at the time of diagnosis was felt likely to be truly infected, with negative Baermann results either reflecting low larval burden and/or intermittent larval shedding. A previous study has found the Angio Detect® test to have good sensitivity (84.3 per cent) and excellent specificity (100 per cent).[4] The sensitivity of Baermann may be limited in cases of intermittent larval excretion, low parasite burden, testing during the prepatent period (although serological testing may also be negative during this time),[5] operator error and/or poor sample quality, and a previous study suggested that serological tests resulted in more consistent results compared with this test.[6]

Advocate™ is licenced for treatment of *A. vasorum* with one or two doses administered 30 days apart and for prevention of *A. vasorum* when applied every four weeks; although the use of a third dose for treatment of infection in one of the dogs which remained positive on Angio Detect® at eight weeks was off label, this was done because there was evidence to suggest ongoing infection in this particular case. Twelve weeks post diagnosis, the dog was found to be negative on Angio Detect® . Despite proven efficacy of between 85.2 per cent and 100 per cent for a single moxidectin/imidacloprid spot-on in the treatment of experimental and natural *A. vasorum* infections,[7 8] one study found that 9 of 10 experimentally infected dogs took between three to seven weeks to become negative on antigen testing following a single treatment with a moxidectin/imidacloprid spot-on and that 1 dog remained infected.[4] Another study[5] found larval excretion to have ceased and Baermann to be negative within three weeks of effective treatment of 16 experimentally infected dogs. In the dog with discordant Angio Detect® and Baermann results at four weeks post-treatment, these findings may have represented a true-negative Baermann result and a delay in the antigen test becoming negative (resulting in the Angio Detect® remaining positive) or treatment failure and either low or intermittent larval shedding resulting in a false-negative Baermann result. The later is supported by the finding of a second positive Angio Detect® result at eight weeks, following the second application of a moxidectin/imidacloprid spot-on to this dog, when a negative Angio Detect® result following effective treatment would have been expected.

Advocate™ is licenced for the treatment of *A. vasorum* in dogs in the UK; under the Cascade this would be one of the first-choice drugs for treatment of this condition. In addition, this medication has proven efficacy for this condition. Approval from an ethical review body was therefore not obtained for this study as primary care veterinary practices would likely have used this treatment protocol even without participation in the study and the case information was anonymised before being submitted to the study.

## CONCLUSIONS

The study found that post-treatment, Angio Detect® testing was concordant with Baermann in seven of the nine dogs. In one of the remaining dogs, Angio Detect® testing was positive and Baermann was negative at diagnosis and in the other dog, this discrepancy was noted at four weeks post-treatment. In both of these dogs, the Baermann result was suspected to be false-negative.

The study also found that application of Advocate™ spot-on solution was an effective treatment for *A. vasorum* infection in dogs and resulted in resolution of the infection based on Angio Detect® testing and Baermann within four weeks, in eight out of nine dogs. One dog required three applications of Advocate™ before testing negative on Angio Detect® .

**Contributors** All authors were involved in the study design but sponsors were not involved in collection of data, study analysis, interpretation or analysis of data. LEB was primarily involved with the acquisition, analysis and interpretation of data for the work. All authors gave final approval of the version to be published.

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**Competing interests** None declared.

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**Data sharing statement** There are no unpublished data from this study.



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