Approaches to Canine Heartworm Disease Treatment Among Alumni of a Single College of Veterinary Medicine

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ABSTRACT

This descriptive study was designed to ascertain the current heartworm treatment strategies employed by veterinary graduates of a single college of veterinary medicine, to assess the frequency with which each of these treatment strategies is prescribed, and to report the motivation behind the use of these treatment strategies. A survey containing a combination of multiple-choice and open-ended questions was distributed via e-mail with an online link during 2013 to graduates of the University of Georgia College of Veterinary Medicine. Demographic data and opinions regarding treatment for cases of canine heartworm disease (HWD) were obtained, and motivation for recommending different treatment strategies was assessed. Nearly all 170 respondents (99%) indicated that they recommend melarsomine dihydrochloride for first-line treatment of canine HWD. Exercise restriction (80%) and monthly heartworm preventive (75%) were components of the treatment approach to HWD with no clinical signs. The majority of respondents (74%) indicated that when first-line treatment recommendations were declined, they endorsed long-term administration of ivermectin (i.e., “slow-kill” method) despite current American Heartworm Society guidelines that recommend against the use of long-term macrocyclic lactone administration for the monotherapy treatment of canine HWD. Respondents also indicated that owners’ financial concerns frequently result in modification of HWD treatment. Routine inclusion of exercise restriction is commonly, but not universally, utilized and may represent an opportunity for improvement in the management of this disease. In addition, when first-line recommendations for heartworm disease treatment are declined, a two-dose melarsomine protocol instead of the slow-kill method should be considered. (J Am Anim Hosp Assoc 2018; 54:246–256. DOI 10.5326/JAAHA-MS-6601)

Introduction

The dog is a highly susceptible host to Dirofilaria immitis, the causative agent of heartworm disease (HWD). Maturation of these worms in the infected dog creates a disease syndrome that includes respiratory signs, cor pulmonale, and right-sided congestive heart failure. In severe and/or untreated cases, HWD can also damage other noncardiopulmonary body systems and ultimately cause death. The disease is considered preventable with the administration of safe, effective macrocyclic lactones (e.g., ivermectin, milbemycin, moxidectin, and selamectin). In spite of the availability of these preventive agents, surveys indicate between 1.2 and 48% of dogs tested by primary care veterinarians are positive for adult...
heartworm infection, with prevalence estimates varying widely due to differences in study design and geographic location.\textsuperscript{2–5} Despite veterinary recommendations for preventive protocols, poor owner compliance contributes to the persistence of this disease. In a 2003 study conducted by the American Animal Hospital Association, veterinarians estimated that 70% of their patients were receiving appropriate heartworm prophylaxis. However, when dispensed heartworm doses were calculated per patient, only 48% of these patients obtained the recommended and prescribed heartworm preventive.\textsuperscript{6} In another study, 76% of dogs presented to the University of Pennsylvania Ryan Veterinary Hospital between January 1999 and December 2006 were recorded as having received heartworm prophylaxis year-round.\textsuperscript{7} Given the clinical significance and prevalence of this disease, the prevention and effective treatment of canine HWD are important concerns in small animal veterinary practice.

For adulticidal treatment of canine HWD, the American Heartworm Society (AHS) currently recommends a three-dose regimen of melarsomine dihydrochloride\textsuperscript{8} combined with doxycycline, preventive doses of macrocyclic lactones, anti-inflammatory doses of glucocorticoids, and exercise restriction.\textsuperscript{8} The three-dose melarsomine protocol has proved quite effective, resulting in 98% worm death based on the results of one study.\textsuperscript{8} A second adulticidal treatment protocol includes a two-dose regimen of melarsomine, although this is no longer recommended as the ideal treatment regimen by the AHS.\textsuperscript{8} In considering the use of either the two- or three-dose melarsomine regimen, as well as the incorporation of doxycycline, macrocyclic lactones, steroid administration, and exercise restriction, the practitioner has several adulticidal treatment protocols from which to choose. Furthermore, some practitioners may forgo the use of melarsomine altogether, opting for a treatment approach that has come to be known as the slow-kill method.

Slow-kill is a term used to describe heartworm treatment protocols that utilize continuous monthly administration of prophylactic doses of one of the macrocyclic lactones, with or without the addition of doxycycline. The long-term monthly administration of the macrocyclic lactone, ivermectin, has been shown to be adulticidal but requires up to 36 mo for complete \textit{D. immitis} elimination.\textsuperscript{9} During this period of monthly drug administration, continued pulmonary and cardiac damage occur. A study of naturally infected dogs treated with monthly ivermectin showed worsening of radiographic pulmonary disease, leading the authors to conclude that slow-kill methods are ill-advised.\textsuperscript{10} Another study of experimentally infected dogs treated with monthly ivermectin showed that 25 of 31 dogs had evidence of pulmonary embolism at necropsy.\textsuperscript{11} Due to the extended opportunity for cardiovascular and pulmonary pathology, the AHS recommends against slow-kill methods for the treatment of canine HWD.\textsuperscript{8}

The objectives of the present study were to gather information on veterinary practitioners’ treatment recommendations for dogs affected by HWD who are presented with and without clinical signs, to determine how often these recommendations agree with AHS guidelines, and to identify the frequency with which owner financial constraints lead to modification of these recommendations. We elicited information about the frequency with which slow-kill methods are recommended in veterinary practice and how often they are used as alternatives to the recommended melarsomine-based protocols. We also sought to determine practitioners’ potential motivations for the use of slow-kill methods. For this purpose, we developed an online survey that included questions concerning HWD treatment regimens. Alumni from the University of Georgia, College of Veterinary Medicine were chosen to participate in the study based upon access to e-mail addresses and ease of survey distribution.

\textbf{Materials and Methods}

The survey consisted of an online questionnaire that was composed of 19 multiple-choice questions and 6 open-ended questions regarding respondent demographic information, treatment of HWD with and without clinical signs, and veterinarian opinions toward slow-kill treatment methods. The questionnaire is available in its entirety online. The survey was approved by the University of Georgia Institutional Review Board (2013-10828-0). The questionnaire was not pretested with any specific groups prior to distribution because the questions were unambiguous. The survey was distributed to e-mail addresses in the spring of 2013 to all graduates of the University of Georgia, College of Veterinary Medicine, regardless of the geographical area in which they practiced. E-mails were obtained from the University Public Relations Office. No signature was required for consent. An informational message was provided with both the initial and 2 wk follow-up e-mail to participate in the survey. Inclusion criteria required that respondents completed the survey in full and that respondents were currently practicing veterinary medicine. Responses were collected through an online survey website\textsuperscript{b} that allows files to be stripped of sender-identifying information. Utilizing the online survey and a separate commercially available application\textsuperscript{b}, all responses were downloaded into spreadsheet format. A standard statistical software program\textsuperscript{d} was utilized for statistical analysis. Some of the open-ended questions consisted of the number of animals with a condition or characteristic. This data was treated as continuous and was tested for normality using the Shapiro-Wilk test. Measures of central tendency and dispersion for nonnormally distributed data were reported as median,
minimum, and maximum. Contingency tables were developed for different combinations of each of the categorical variables obtained in response to the multiple-choice questions. Data was sparse for some graduation years; therefore, year of graduation was redefined as a categorical ordinal variable as follows: graduation prior to or during/after the year 2000. The graduation year was evaluated for an association between graduation year and opinions regarding the slow-kill method. The median number of animals treated or the number of heartworm-positive cases was used as a cutoff point to create a binomial variable. The \( \chi^2 \) or Fisher exact tests were used for categorical data. The alpha value was set at \( P \leq 0.05 \).

**Results**

**Respondents**

A total of 2,000 graduates were identified to participate in the survey, of whom 1,924 had a valid e-mail address on file. Of these 1,924, 654 graduates (34%) opened the invitation. The 2 wk reminder e-mail was sent to 1,932 e-mail addresses, of which 1,919 were valid. Of those with valid e-mail addresses, a total of 507 graduates (26%) opened this reminder e-mail. The survey was closed 1 mo after the initial invitation. A total of 170 veterinarians completed the online survey. Three respondents were excluded from analysis because they were not currently practicing veterinary medicine at the time they responded. The overall response rate of those who opened the initial invitation e-mail was 170/654 (26%). The median number of years since graduation of respondents was 10 yr (minimum–maximum, 0–59 yr; Figure 1). The year of graduation for respondents ranged from 1954 to 2013, and the largest percentage of respondents graduated in 2012 (9.5%). Respondents were not asked to report the city or state in which they were practicing veterinary medicine at the time of the survey. The majority of respondents (65%) indicated that they practice in suburban areas, with the balance divided between metropolitan (28%) and rural (7%) regions. Most respondents (81%) indicated that they work in privately owned practices, with the remainder divided between corporately owned (12%), academic (4%), shelter (2%) and “other” (1%) practices. Finally, the majority (95%) of respondents indicated that they work in small animal practices. A small total percentage of respondents reported that they work in mixed animal (5%) or exotic animal (0.6%) practices.

Respondents reported a median canine caseload of 2,000 cases/year (minimum–maximum, 100–15,000). The estimated median number of heartworm-positive dogs diagnosed annually was 10 cases/year (minimum–maximum, 0–1,500). Respondents indicated that most dogs diagnosed with HWD each year either had no available history regarding administration of heartworm preventive (38%) or had never been given heartworm preventive (34%). Less frequently, respondents reported that heartworm-positive dogs were given heartworm preventive seasonally with one or more missed doses (17%) or had been given year-round heartworm preventive with one or more missed doses (11%).

**HWD Cases with No Clinical Signs**

Respondents were asked to identify which of a provided list of options were components of their first-line treatment approach to cases of HWD characterized by no clinical signs, assuming no financial constraints or medical contraindications. Options provided included the following: exercise restriction, monthly heartworm preventive, doxycycline, two-injection melarsomine protocol, three-injection melarsomine protocol, corticosteroids, and aspirin. Respondents were also asked to specify any routinely recommended treatments that were not included in this list. In cases of HWD with no clinical signs, all respondents indicated that they recommend some form of treatment (Figure 2A). The vast majority (99%) of respondents reported the use of melarsomine as part of their first-line therapy, with 76% using a three-dose melarsomine protocol (one intramuscular injection followed 1 mo later by two doses 24 hr apart) and the minority (24%) using a two-dose melarsomine protocol (two intramuscular injections of melarsomine, 24 hr apart). Most respondents (99%) indicated that they use melarsomine in conjunction with other therapies, including exercise restriction (81%), monthly heartworm preventive (75%), and doxycycline (77%). Of respondents who reported the use of melarsomine as part of first-line therapy, only 9.5% reported that they use melarsomine as a single-agent treatment. Only 1% of respondents reported that they
do not recommend melarsomine as a component of their first-line therapy for canine HWD; reasons cited by these respondents included belief in the superior efficacy of the slow-kill method (2/167), difficulty stocking melarsomine (1/167), and preference for levamisole as both an adulticide and as a microfilaricide in all HWD cases (1/167).

Overall, reported first-line treatment approaches to cases of HWD with no clinical signs among individual veterinarians were highly variable, with 30 different reported management permutations. The most frequently reported single treatment combination included melarsomine in a three-dose protocol with heartworm preventive and doxycycline (55%). The next most frequent combinations were melarsomine in a two-dose protocol with heartworm preventive and doxycycline (13%), followed by melarsomine in a three-dose protocol with doxycycline (8%; Figure 3).

Respondents were asked to identify which of the same provided list of options were components of their second-line treatment approach to cases of HWD with no clinical signs, when first-line treatment recommendations were declined (Figure 2B). The majority of respondents (74%) reported that they recommend slow-kill approaches as second-line therapy. For slow-kill methods, monthly heartworm preventive was preferentially used in combination with doxycycline (75%) rather than alone (25%). Most respondents (94%) who reported that they recommend a slow-kill method as second-line therapy for cases of HWD without clinical signs also indicated that they recommend a melarsomine-based protocol as their first-line approach. Of these respondents who reported they recommend a slow-kill method as a second-line treatment, all (100%) indicated a belief that slow-kill methods are associated with fewer adverse events than are melarsomine-based protocols. Only 20% of respondents reported they recommend a two-injection melarsomine protocol as second-line therapy. Approximately 4% of respondents reported that their second-line treatment approach consists of a three-dose melarsomine protocol. Some respondents reported that they do not alter their first-line treatment recommendations and try to make the recommended approach more affordable if declined (2%).

HWD Cases with Clinical Signs
Next, respondents were asked to identify which of a provided list of options were components of their first-line treatment approach to cases of HWD with clinical signs, assuming no financial constraints...
or medical contraindications. Again, all respondents indicated that they recommend some form of treatment for these cases (Figure 4A). As for patients displaying no clinical signs, the majority (99%) of respondents reported that they recommend melarsomine-based protocols as a component of first-line therapy. The majority (95%) reported that they recommend a three-dose melarsomine protocol, whereas only 5% indicated that they utilize a two-dose melarsomine protocol. Most respondents (90.5%) indicated that they prescribe therapies in addition to melarsomine, including exercise restriction (88%), monthly heartworm preventive (75%), doxycycline (81%), corticosteroids (58%), and aspirin (10%) as components of first-line therapy for cases of HWD with clinical signs (Figure 4A). Among the 1% of respondents who reported that they do not recommend melarsomine for first-line therapy in cases of HWD with clinical signs, reasons cited included the belief that slow-kill methods are associated with fewer adverse events (1/167), and preference for levamisole as both an adulticide and as a microfilaricide in all HWD cases (1/167).

The first-line treatment approaches to cases of HWD with clinical signs were highly variable, with 27 different reported management permutations. The most frequently reported treatment combination included melarsomine in a three-dose protocol with heartworm preventive and doxycycline (65%). The next most frequently recommended combination included melarsomine in a three-dose protocol with doxycycline (12%), followed by melarsomine in a two-dose protocol with heartworm preventive and doxycycline (3%; Figure 5).

The proportion of veterinarians reporting the use of furosemide, enalapril, sildenafil, antibiotics, tramadol, nonsteroidal anti-inflammatory drugs, corticosteroids, and/or clopidogrel in cases with clinical signs (69%) was statistically different from that of the cases with no clinical signs (38%; P < .0001). The proportion of veterinarians prescribing corticosteroids in patients with clinical signs (58%) was statistically different from the proportion of veterinarians prescribing corticosteroids in patients exhibiting no clinical signs (37%, P = .05). However, there was no statistically significant difference in the reported frequency of doxycycline use between cases with clinical signs (79%) and those without (81%; P = .56).

Respondents were asked to identify which of the same provided list of options were components of their second-line therapy for cases of HWD with clinical signs, when first-line treatment recommendations were declined (Figure 4B). The majority of respondents (73%) reported that they utilize slow-kill approaches as second-line therapy; of these, 90% indicated they incorporate both monthly heartworm preventive and doxycycline. Almost all respondents who reported that they recommend a slow-kill method as second-line therapy for cases of HWD with clinical signs indicated they recommend a melarsomine-based protocol (94%, three-injection protocol; 5%, two-injection protocol) with exercise restriction (90%) as their first-line approach. Only 21% of respondents reported that they recommend a two-injection melarsomine protocol as second-line therapy; each of these respondents reported that they recommend a three-dose melarsomine protocol as first-line therapy. A small percentage (2%) of respondents reported that they recommend a three-injection melarsomine protocol as second-line therapy. These respondents also reported that they recommend a three-injection melarsomine protocol for their first-line approach and do not change strategies based upon rejection of their first-line approach. A small number of respondents (3%) reported that their second-line treatment approach consists of exercise restriction either alone, with aspirin, or as a combination therapy with
doxycycline and corticosteroids. Some respondents reported that they do not alter their first-line treatment recommendations and try to make the recommended approach more affordable if declined (1%).

Of the respondents whose first-line treatment approach to cases of HWD with clinical signs was based upon three-dose melarsomine protocols, a two-injection protocol was reported to be recommended as second-line therapy by only 21% of respondents. As for cases without clinical signs, the majority of respondents reported that they recommend slow-kill methods as second-line therapy. Ninety percent of respondents who indicated that they prefer to utilize a two-dose melarsomine protocol for first-line treatment of cases of HWD associated with clinical signs indicated they recommend slow-kill protocols when their first-line recommendations are declined.

Respondents were asked to estimate the frequency with which particular factors lead to modification of first-line treatment approaches. Most respondents (96%) reported that when first-line approaches were declined, owner financial concerns were cited as the causative factor. Owner financial concerns were reported to cause modification of treatment recommendations in a median of 50% (minimum–maximum, 0–100%) of cases. A small number of respondents (4%) reported that owner financial concerns were never a causative factor for treatment modification. Several respondents (2%) reported that a recent increase in the price of doxycycline has contributed to alterations in their treatment recommendations.

**Slow-Kill Treatment Methods**

Respondents were asked to share their opinions regarding slow-kill methods. First, respondents were asked about the efficacy of slow-kill methods in elimination of heartworm infection. Seventy-one percent of respondents reported that they disagree with the statement that the slow-kill method is as effective as melarsomine therapy in eliminating heartworm infection and producing a negative heartworm antigen test result. Eleven percent of respondents reported that they do not feel as though they can compare the efficacies of slow-kill methods and melarsomine therapy. Of the 18% of respondents who agree with the statement that slow-kill methods are as effective as melarsomine therapy at eliminating adult heartworms, 52% and 77% reported that they recommend a three-injection melarsomine protocol as part of their first-line therapy for cases of HWD without and with clinical signs, respectively. Of the 18% of respondents who agree with the statement that slow-kill methods are as effective as melarsomine therapy at eliminating heartworm infection, 45% and 13% reported
that they recommend a two-injection melarsomine protocol as part of their first-line therapy for cases of HWD without and with clinical signs, respectively. In order to ascertain whether these opinions might have been influenced by the time period during which respondents attended veterinary school, responses were grouped according to year of graduation (prior to, or during/after, the year 2000). The proportion of veterinarians, grouped according to year of graduation, was not associated with the belief that the slow-kill method is as effective as melarsomine in eliminating infection ($P = .68$). The proportion of veterinarians grouped according to the reported number of heartworm cases treated yearly ($\leq 10$ cases/year versus $>10$ cases/year) was not associated with the belief that the slow-kill method is as effective in eliminating heartworm infection ($P = .40$).

Next, respondents were asked about the efficacy of slow-kill methods in resolution of clinical signs. Seventy-nine percent of respondents reported that they disagree with the statement that slow-kill methods are as effective as melarsomine therapy in resolving clinical signs associated with HWD. Fifteen percent of respondents reported that they do not feel they can compare the resolution of clinical signs following use of slow-kill methods and melarsomine therapy. Of the 6% of respondents who reported that they agree with the statement that slow-kill methods are as effective as melarsomine therapy in resolving clinical signs, 36% and 90% reported that they recommend a three-injection melarsomine protocol as part of their first-line therapy for cases of HWD without and with clinical signs, respectively. Of the 6% of respondents who reported that they agree with the statement that slow-kill methods are as effective as melarsomine therapy in resolving clinical signs, 36% and 0% indicated they recommend a two-injection melarsomine protocol as part of their first-line therapy for cases of HWD without and with clinical signs, respectively. When respondents were grouped by year of graduation, as described above, there was no association between graduation year and the belief that slow-kill methods are as effective as melarsomine therapy in resolving clinical signs ($P = .47$). In addition, when respondents were grouped by reported caseload, as described above, there was no significant association between the number of heartworm-positive cases that respondents reported treating yearly and their belief that the slow-kill method is effective in eliminating clinical signs ($P = .47$).

Finally, respondents were asked their opinions regarding the relative safety of slow-kill methods and melarsomine therapy for the treatment of canine HWD. Twelve percent of the total number of respondents indicated that they believe slow-kill methods are safer than melarsomine therapy, whereas 79% indicated they do not believe that slow-kill methods are safer. Ten percent of respondents indicated that they are unable to compare safety between slow-kill methods and melarsomine therapy. Of the respondents who indicated a belief that slow-kill methods are safer than melarsomine-based protocols, 68% and 80% reported that they recommend a three-injection melarsomine protocol as part of their first-line therapy for HWD without and with clinical signs, respectively. Twenty-six percent and 10% of these respondents reported that they recommend a two-injection melarsomine protocol as part of their first-line therapy for patients without and with clinical signs, respectively. Grouping veterinarians’ responses according to year of graduation revealed no apparent association between graduation year and opinions regarding the relative safety of slow-kill and melarsomine-based methods of therapy for the treatment of canine HWD ($P = .98$). There was no significant association between the number of heartworm cases that respondents reported treating yearly and their belief that the slow-kill method is safer than melarsomine therapy ($P = .47$).
Discussion

This study reveals information regarding the ways in which a sample of veterinarians treats canine HWD. All respondents reported that they recommend therapy for HWD patients, regardless of the presence or absence of clinical signs. Protocols varied, but the majority of respondents reported that their first-line therapy includes melarsomine for both categories of patients. In general, respondents also reported that they employ exercise restriction, heartworm preventive therapy, and doxycycline as components of their first-line therapeutic approach, and that they employ ancillary medications more commonly for patients with clinical signs. When first-line therapy is declined, the majority of respondents indicated that they employ slow-kill protocols of heartworm preventive plus doxycycline as second-line therapy. Respondents cited owner financial constraints as the predominant reason for modification of their first-line medical recommendation. Finally, most respondents indicated they believe that slow-kill approaches are less effective at eliminating infection and resolving clinical signs of HWD than melarsomine-based protocols, and that slow-kill methods are not safer than melarsomine-based protocols.

Owner financial concerns were reported to cause modification of treatment recommendations in a median of 50% (minimum–maximum, 0–100%) of cases. Although additional nonfinancial considerations likely contribute to modification, questions designed to ascertain these factors were not included in the questionnaire. It could be hypothesized, for example, that misinformation provided to clients by sources other than veterinary practitioners may influence owner-driven decisions to use slow-kill methods. The origin of client interest in slow-kill methods is a matter that requires further investigation. Given the relatively high frequency with which financial constraints alter treatment protocols, it may be prudent for veterinarians to discuss with pet owners the potential complications of and financial costs associated with slow-kill therapy, as this approach was reportedly offered as a second-line treatment recommendation in 74% of cases without clinical signs and 64% of cases with clinical signs. Alternatively, a protocol including two doses of melarsomine, administered 24 hr apart (per label instructions) may be considered the most judicious use of limited financial resources when a full three-dose treatment regimen is not feasible, as this protocol has a reported efficacy in excess of 96%.4

Although most respondents reported that they recommend exercise restriction as a component of first-line HWD therapy for dogs with and without clinical signs, a sizable minority (12% and 19%, respectively) indicated that they do not. Current AHS guidelines state that exercise restriction during the treatment and recovery period of HWD is essential for minimizing cardiopulmonary complications such as pulmonary thromboembolism.8,12 A study of experimentally infected dogs who were either exercise-restricted or allowed moderate activity showed that dogs who were exercise-restricted took longer to exhibit clinical signs of HWD and developed less histologic evidence of pulmonary arterial vascular damage.13 Exercise or strenuous activity increases blood flow to already damaged arterioles and capillary beds, resulting in further capillary wall destruction and leading to fibrotic change in the pulmonary beds. Subsequently, pulmonary vascular resistance can increase and cor pulmonale may result.13,14 If exercise restriction is not imposed during HWD treatment, it is possible that adverse events may be seen more frequently. Respondents who reported they do not recommend exercise restriction may be unaware of these risks. Respondents may not recommend exercise restriction because they presume that owner compliance with such a recommendation would be low. The findings of this study reveal an opportunity to increase the utilization of exercise restriction, which is both inexpensive and risk-free.

A predominate component of first-line HWD therapy was reported to include monthly heartworm preventives. However, a sizable number of respondents (25%) reported that they do not include monthly heartworm preventives as part of HWD therapy. The use of a macrocyclic lactone for 2–3 mo prior to melarsomine administration is recommended by the AHS to allow larvae to mature to an age typically susceptible to melarsomine (i.e., decrease the susceptibility gap) before melarsomine administration.8,15 Alternatively, they may have concerns for anaphylactic reactions secondary to microfilarial death following administration of macrocyclic lactones or with historical diethylcarbamazine administration.8,16 The findings of this study reveal an opportunity to increase awareness of the value of heartworm preventive therapy as part of HWD treatment protocols, and raise awareness of strategies to mitigate the risk of anaphylactic reactions, among practicing veterinarians.

The use of doxycycline to kill Wolbachia, an endosymbiont of Dirofilaria immitis, is recommended by the AHS to decrease both heartworm fertility and transmission of infective stages to other dogs via the mosquito vector.8,17–23 When given within 1–2 mo following heartworm infection, doxycycline has been shown to reduce the number of third- and fourth-stage larvae in experimental studies.8 Doxycycline administration also decreases melarsomine-associated pulmonary thromboembolism and enhances the killing of adult heartworms.1 Although most respondents (80%) in the present study reported that they prescribe doxycycline as part of their first-line treatment recommendations for cases of HWD with or without clinical signs, the remainder represent a substantial percentage of practitioners who do not report adherence to AHS guidelines.
Around the time the survey was administered, the cost of doxycycline had increased considerably, a fact that may have affected the treatment recommendations of some respondents, despite the fact that respondents were asked to assume no financial limitations when describing their recommendations. This finding reveals an opportunity to increase the use of this beneficial therapy.

Respondents indicated the use of adjunct medications more commonly for patients with HWD characterized by clinical signs than for those without clinical signs. Specifically, 58% and 37% of respondents reported they utilize corticosteroids in patients with and without clinical signs, respectively. Corticosteroids are recommended by the AHS to help control signs of pulmonary thromboembolism, to reduce the potential for anaphylaxis in the microfilaricemic patient, and to help control inflammation associated with worm death secondary to melarsomine injection. It seems plausible that veterinarians reported the greater use of steroids in patients exhibiting clinical signs because of a greater concern for the risks mentioned by the AHS.

Respondents reported the use of aspirin as a component of first-line HWD therapy for dogs with (10%) and without clinical signs (3%). The current AHS guidelines do not recommend aspirin due to conflicting evidence to support its use and the potential for detrimental effects. In one investigation, no difference in histopathologic lesion severity was identified between the lungs of experimentally infected heartworm-positive dogs treated with or without aspirin. Another study of aspirin’s effect on platelet adhesion to chronically damaged pulmonary arterioles among HWD dogs documented enhanced platelet adhesion to the damaged vascular surface after 4 days of therapy, but decreased platelet adhesion after 30 days, compared with untreated dogs. Given the conflicting results of these studies, and the theory that high-dose aspirin may inhibit endothelial cell cyclooxygenase and cause vasoconstriction, thereby favoring platelet adhesion, aspirin is not currently recommended by the AHS for HWD treatment.

The majority of respondents cited financial constraints as the most common reason that first-line recommendations require modification. Interestingly, there was no evidence to support the idea that a three-dose melarsomine protocol was modified to a less expensive two-dose melarsomine protocol in a large number of cases in which financial concerns were cited. It is possible that the cost savings of reducing the number of melarsomine doses would be significant to many owners, while still allowing the use of a relatively fast-acting adulticide protocol.

Nearly all respondents in the present study reported that they elect slow-kill methods for the treatment of cases of HWD, regardless of the presence or absence of clinical signs, when first-line recommendations are declined. The combination of macrocyclic lactones and doxycycline has been shown to be adulticidal in dogs with both experimental and naturally acquired HWD, and the combination has been shown to work more efficiently than ivermectin alone. In addition, this combination slows *D immitis* larval development and causes deterioration of existing adult heartworms. However, the slow-kill method is not recommended by the AHS because continuous monthly administration of ivermectin requires up to 36 mo for complete *D immitis* elimination, during which time continued pulmonary and cardiac damage occur. In study dogs who were administered continuous monthly ivermectin 4 mo post infection, approximately 70% of worms were dead after 6 mo and 95.1% were dead after 12 mo. However, when ivermectin was started 8 mo post infection, the efficacy decreased dramatically, with only 56% of worms dead after 16 monthly doses. There are no experimental studies to support the idea that the slow-kill method is safer, associated with fewer adverse events, or more efficacious than melarsomine-based protocols for the treatment of heartworm disease. The slow-kill method is only considered appropriate by the AHS for cases in which melarsomine therapy is contraindicated due to concurrent medical disease, patient age, and/or financial limitations. A melarsomine shortage in 2011 raised questions about alternative treatment approaches to HWD, and the AHS recommended slow-kill methods only while melarsomine was unavailable. Given the continued pulmonary insult that occurs with slow-kill methods, exercise restriction is recommended for the entire duration of slow-kill treatment (>1 yr), which is unlikely to be acceptable to most dog owners. The relatively high number of respondents who report using this pharmacologic option suggests an area where further education and an industry guideline may be beneficial for both practitioner and patient. The authors would suggest that veterinarians consider the two-dose melarsomine protocol as ideal second-line therapy in these situations, although it is acknowledged that there are currently no established guidelines for second-line therapies that address a suitable approach to this common clinical dilemma.

A large number of respondents reported that they believe slow-kill methods are less effective than melarsomine for producing a negative heartworm test result (72%) and for resolving clinical signs (79%). In addition, a large number of respondents (79%) specified that they do not believe slow-kill treatment is safer than melarsomine therapy. These results do not support the idea that veterinary practitioners are worried about the safety of melarsomine use in canine HWD or that the slow-kill method has become more popular as a first-line treatment approach to HWD. However, this study does show that a majority of practitioners who responded to this survey use a slow-kill approach to canine HWD when a three-dose melarsomine protocol is declined.
There are limitations to this study. First, as response to the survey was voluntary, it is possible that the practitioners who responded are not representative of the general population of veterinarians, with self-selection bias potentially introduced by those with a particular interest in, or comfort with, the management of heartworm disease, or by those treating a greater number of heartworm cases yearly. Further, respondents were all graduates of the University of Georgia, College of Veterinary Medicine, and their responses may not be comparable to graduates from other veterinary colleges. Future surveys designed to obtain information from graduates of veterinary schools other than the University of Georgia are warranted. Unfortunately, our survey design did not include questions designed to determine the geographic region in which respondents were practicing at the time of survey completion. Because the incidence of HWD varies geographically, responses may have been influenced by the frequency with which respondents manage this disease. Additional surveys that describe the location of veterinary practice within the United States are justified. Finally, as with any survey-based study, accuracy depends upon candid subject response and accurate recall.

Conclusion
This study was conducted in an effort to advance our understanding of the current heartworm management strategies employed by veterinary practitioners and to compare these practices with AHS guidelines. The present study suggests that the majority of respondents follow AHS guidelines for the treatment of HWD. Overall, few respondents reported that they recommend slow-kill methods for their first-line treatment recommendation of canine HWD, and the majority reported that they feel such protocols are neither more effective nor safer than melarsomine-based protocols. Adjunctive medical therapies, including monthly heartworm preventive, doxycycline, and/or corticosteroids, were reported as frequently prescribed by the respondents of this survey. A minority, but a sizeable percentage, of respondents reported that they use aspirin for cases with clinical signs despite a lack of support for this therapy in the current AHS guidelines. Similarly, a large number of survey respondents reported that they do not include exercise restriction as part of their ideal treatment approach to cases of HWD, regardless of the presence or absence of clinical signs, despite AHS recommendations that support this measure. The findings of this study reveal an opportunity to increase awareness of the value of heartworm preventive therapy as part of HWD treatment protocols and the importance of exercise restriction, through continuing education and the veterinary literature. In addition, the use of aspirin in HWD cases occurs despite current AHS guidelines.

Financial concerns expressed by dog owners were reported to frequently lead to modification of recommendations for the treatment of canine HWD, suggesting that veterinarians should have a backup plan in the event that their first-line recommendations are declined. When first-line treatment recommendations are declined, the majority of respondents reported that they endorse slow-kill methods instead of recommending a two-dose melarsomine protocol. The results of the present study indicate that increased awareness of the benefits of exercise restriction during heartworm treatment is needed among veterinarians and that the two-dose melarsomine protocol should be promoted as an alternative that is more affordable than the three-dose protocol and more effective than slow-kill methods.

Footnotes


