Short communication

# FIRST STUDY ON THE EFFICACY OF ABAMECTIN IN A COMBINED FORMULATION WITH PRAZIQUANTEL AGAINST AELUROSTRONGYLUS ABSTRUSUS IN CATS

## A. TONEV<sup>1</sup>, P. ILIEV<sup>1</sup> & R. MILEVA<sup>2</sup>

<sup>1</sup>Department of Veterinary Microbiology, Infectious and Parasitic Diseases; <sup>2</sup>Department of Pharmacology, Animal Physiology and Physiological Chemistry; Faculty of Veterinary Medicine, Trakia University, 6000 Stara Zagora, Bulgaria

#### **Summary**

Tonev, A., P. Iliev & R. Mileva, 2023. First study on the efficacy of abamectin in a combined formulation with praziquantel against *Aelurostrongylus abstrusus* in cats. *Bulg. J. Vet. Med.*, **26**, No 2, 289–294.

The information about abamectin efficacy in cases of feline aelurostrongylosis is scarce. Six naturally infected cats were treated with combination of abamectin and praziquantel every seven days until two consecutive negative faecal test results. Abamectin was administered at a dose rate of 0.1 mg/kg. For the evaluation of the efficacy, the number of larvae per gram (LPG) was assessed 30 and 60 days after the first treatment by the Baermann's technique. After the first 4 administrations, a rapid decline in LPG was observed and after the 8<sup>th</sup> administration, all animals were free of *A. abstrusus* larvae. Although the results affirm that abamectin may be successfully used in cases of aelurostrogylosis in cats, further clinical studies are needed to validate this pilot investigation.

Key words: Aelurostrongylus abstrusus, cats, abamectin, macrocyclic lactone

Aelurostrongylosis is a helminthosis in cats, characterised by a variety of clinical signs – from asymptomatic infection to severe respiratory distress with weight loss (Giannelli et al., 2017; Borisov et al., 2018). It is caused by the small nematode Aelurostrongylus abstrusus (Railliet, 1898) from the Angiostrongylidae family. A. abstrusus is globally distributed. The domestic cat (Felis silvestris catus) is

considered a natural host and animals of both genders and all ages may become infected (Barutzki & Schaper, 2013; Elsheikha *et al.*, 2016; Traversa *et al.*, 2021).

The primarily used antinematode drugs for control of aelurostrongylosis include fenbendazole, selamectin and combined formulations with milbemycin oxime, moxidectin, eprinomectin and

emodepside (Bohm et al., 2015; Traversa & Di Cesare, 2016). Extra-label use of ivermectin has also been reported (Foster et al., 2004). Abamectin is a macrocyclic lactone approved for use in veterinary medicine (Shoop & Soll, 2002). It stimulates the release of gamma-aminobutyric acid (GABA), hindering the transmission of nerve impulses, causing paralysis of nematodes, insects and ticks (Martin et al., 2002). Abamectin has a similar efficacy spectrum to ivermectin (including most species of gastrointestinal nematodes), although data about its activity against ectoparasites are more limited in comparison to ivermectin (Shoop & Soll, 2002). In order to expand the anthelmintic spectrum, it could be combined with praziquantel as anticestode drug (Chai, 2013). Their ready to use combination is licensed in Bulgaria and other EU countries (Anonymous, 2021).

The information about abamectin activity against *A. abstrusus* is limited. Considering the lack of data on abamectin spectrum of activity, the aim of the current study was to test its efficacy after oral administration in cats with aelurostrongylosis.

In the period 2019–2021 clinical examinations of cats (n=6) from Southeastern Bulgaria were performed at the Small Animal Clinic of Trakia University, Bulgaria. Based on anamnesis data (outdoor access, lack of deworming) and respiratory symptoms, the animals were subjected to coprological examination. All cats were positive for infection with A. abstrusus. Considering the inability to control the treatment, the prevention of spreading the infection and the relatively long period of treatment, owners gave their informed consent for hospitalisation of their pets in the Small Animal Clinic's isolation ward. Cats were of mixed breeds and non-vaccinated. Five animals were male and one – female. Their mean age was 21 months (range 4–96 months). Two of the cats showed severe respiratory symptoms, including dyspnoea, cough, wheezing and nasal discharge. The other four animals had mild to absent respiratory symptoms. Three of the cats had diarrhoea.

Baermann's technique for detection of *A. abstrusus* first stage larvae (Zajac & Conboy, 2012) was used for determining the intensity of invasion before and after the treatment. Briefly, faecal samples were placed into Baermann funnels, filled with 50 mL warm tap water. After 24 h the liquid was collected into a tube and centrifuged at 2500 rpm for 5 min. The supernatant was removed and the sediment was examined on a microscope slide. The larvae were counted and identified to species level. Thereby, the number of larvae per gram (LPG) and the presence of coinfections were recorded.

Toxocara cati was detected in all animals. Prior to the trial Cystisospora spp. oocysts and Ancylostoma spp. eggs were found in three and four cats, respectively, by using faecal flotation with saturated sodium chloride (Zajac & Conboy, 2012). Three animals shed Dipylidium caninum proglottides during the examinations or after the start of the treatment. Additionally, before the beginning of the experiment whole blood and faecal samples were obtained from all animals. The blood was tested with SNAP Combo Test (IDEXX lab., USA) and faeces: with FeliD-3 Ag (Bionote, Corea) respectively, according to manufacturer's instuctions. All cats were negative for FIV and FeLV, and for FeCoV and FPV infections. After testing whole blood samples with SNAP 4Dx Plus Test (IDEXX lab., USA) antibodies against Anaplasma nla-

tys/Anaplasma phagocytophilum, Ehrlichia canis/Ehrlichia ewingii, and Borrelia burgdorferi or antigens of Dirofilaria immitis were not found in any of the animals.

Based on positive results for aelurostrongylosis, Prazimec C was administred orally every 7 days at a dose of 1 tablet per 2.5 kg body weight, corresponding to 0.1 mg/kg abamectin and 2.5 mg/kg praziquantel. During the trial cats had free access to water and commercial dry food. Animals were observed daily for side effects such as tremor, vomiting and changes in general condition. The treatment continued until two consecutive negative faecal test results. The efficacy of the treatment on day 30 and 60 after the beginning of repeated administration was calculated as percentage using the following formula (Vercruysse et al., 2001; 2002; Knaus et al., 2014):

Efficacy (%) = 
$$(N1 - N2)/N1 \times 100$$
,

where N1: the number of larvae before the treatment; N2: the number of larvae after the administration of the tablets.

Due to the poor general health condition, a supportive therapy was included in the treatment protocol of four cats. It consisted of butaphosphan and Vitamin B12 (Catosal 10%, Bayer Animal Health, Germany); Vitamins A, D3 and E (AD3E,

Vetprom, Bulgaria) and Vitamin C (Vitamin C, Biovet, Bulgaria). Systemic antimicrobial therapy in the same animals was performed with amoxicillin/clavulanic acid (Synulox, Zoetis, USA) at a dose of 8.75 mg/kg bw, subcutaneously, once daily for 5–15 days, because of the presence of bronchitis or pneumonia on radiographic evaluation.

Differences in the number of L1 between day 0 and day 30 and between day 0 and day 60 after the start of repeated administration were tested for statistical significance (STATISTICA 10.0, StatSoft, Tulsa, USA).

The results from the treatment revealed no side effects e.g. vomiting, loss of appetite or tremor. All cats demonstrated improvement in the general health condition and at day 60 they showed no clinical signs. Results of faecal examinations in progress are summarised in Table 1.

All animals received a total of 4 to 8 doses of abamectin/praziquantel combination. After the first administration, a rapid decline in the number of larvae was observed. An exception was cat No. 2 which showed an increased number of LPG at day 30 after the start of the trial. Cat No. 5 stopped shedding larvae after the fourth treatment. Although there was a clear tendency towards reduction of average num-

**Table 1**. Aelurostrongylus abstrusus larval counts (larvae per gram) before and after first administration (AFA) of abamectin at a dose rate of 0.1 mg/kg in cats (n=6) and percentage efficacy

Cat	LPG before treatment	LPG 30 days AFA	Efficacy 30 days AFA (%)	LPG 60 days AFA	Efficacy 60 days AFA (%)
1	290	282	2.76	0	100
2	97	108	-11.34	0	100
3	393	48	87.79	0	100
4	3	1	66.67	0	100
5	503	0	100.00	0	100
6	402	21	94.78	0	100

ber of LPG at day 30 after first administration (AFA) in comparison to their number before the start of the experiment (281 vs 77; P>0.05). The efficacy 30 days AFA varied between -11.34% and 100%. At day 60 AFA no *A. obstrusus* larvae were found in any of the animals. This decrease was statistical significant (P<0.05).

Aelurostrongylosis is a mostly neglected parasitic disease in cats. However, in recent years its clinical significance and wide recognition is becoming apparent (Elsheikha et al., 2016). In accordance with previous studies (Borisov et al., 2018), this report confirms the presence of aelurostrogylosis in cats in Bulgaria. Despite the availability of effective drugs such as milbemycin oxime, moxidectin, eprinomectin and emodepside (Knaus et al., 2014; Bohm et al., 2015; Traversa & Di Cesare, 2016) against this helminthiasis, there are cases of lack of efficacy. Grandi et al. (2005) reported unsatisfactory results after therapy with selamectin. The combined spot-on formulations may be convenient and effective (Traversa & Di Cesare, 2016), but are usually expensive. Available data about abamectin efficacy against A. obstrusus is limited to one study. Foster et al. (2004) report the usage of two doses of the drug (300 µg/kg) two weeks apart in a cat with aelurostrongylosis. They consider the case resolved without providing more detailed information about intensity of invasion and criteria used. There are neither data on abamectin pharmacokinetics in cats or dogs, nor information on the effective plasma and lung concentrations which should be achieved. Available information on the pharmacokinetics of this drug is limited to several studies on parenteral and oral administration of abamectin in ruminants (Cerkvenik-Flajs et al., 2007;

Zele et al., 2011; Singh et al., 2018; Ballent et al., 2020).

The limitations of the investigation on the efficacy of combination of abamectin and praziquantel in cats naturally infected with A. obstrusus after repeated oral administration were related to the low number of cats resulting in high variations in the assessment of the efficacy. Complete elimination of the infection was observed after 4-8 applications. These pilot results point out that abamectin may be effective in cases of aelurostrogylosis in cats, but the duration of therapy should depend on the faecal findings until full elimination of parasite's larvae. The presented data can be used in future studies for validation of the dosing regimen.

#### REFERENCES

Anonymous, 2021. Register of VMPs licensed for use in the Republic of Bulgaria, https://www.bfsa.bg/userfiles/files/VMP/R eg/2021/%20%D0%B0%D0%BA%D1%8 2%D1%83%D0%B0%D0%BB%D0%B5 %D0%BD%20%D0%BA%D1%8A%D0%BC%2030%20OKTOMVRI%202021%20 pdf.pdf (26 April 2021 date last assessed) (BG).

Ballent, M., C. Canton, P. Dominguez, G. Bernat, C. Lanusse, G. Virkel & A. Lifschitz, 2020. Pharmacokinetic-pharmacodynamic assessment of the ivermectin and abamectin nematodicidal interaction in cattle. *Veterinary Parasitology*, 279, 109010

Barutzki, D. & R. Schaper, 2013. Occurrence and regional distribution of *Aelurostrongylus abstrusus* in cats in Germany. *Parasitology Research*, **112**, 855–861.

Böhm, C., S. Wolken, M. Schnyder, W. Basso, P. Deplazes, A. Di Cesare, K. Deuster & R. Schaper, 2015. Efficacy of emodepside/praziquantel spot-on (Profender®) against adult *Aelurostrongylus abstrusus* nematodes in experimentally infected cats.

- *Parasitology Research*, **114**, Suppl. 1, S155–S164.
- Borisov, B., R. Rafailov, D. Hadzhimitev, G. Marinov, N. Zlateva & E. Magkriot, 2018. Aelurostrongylus abstrusus in cats – diagnosis and treatment. Tradition and Modernity in Veterinary Medicine, 3, 91–96.
- Cerkvenik-Flajs, V., I. Grabnar, N. Kozuh Erzen, I. Marc, J. Antonić, A. Vergles-Rataj, J. Kuzner & M. Pogacnik, 2007. Kinetics of abamectin disposition in blood plasma and milk of lactating dairy sheep and suckling lambs. *Journal of Agricultu*ral and Food Chemistry, 55, 9733–9738.
- Chai, J. Y., 2013 Praziquantel treatment in trematode and cestode infections: An update. *Infection & Chemotherapy*, 45, 32–43.
- Elsheikha, H. M., M. Schnyder, D. Traversa, A. Di Cesare, I. Wright & D. W. Lacher, 2016. Updates on feline aelurostrongylosis and research priorities for the next decade. *Parasites & Vectors*, **9**, 389.
- Foster, S. F., P. Martin, G. S. Allan, V. R. Barrs & R. Malik, 2004. Lower respiratory tract infections in cats: 21 cases (1995–2000). *Journal of Feline Medicine and Surgery*, **6**, 167–180.
- Giannelli A., G. Capelli, A. Joachim, B. Hinney, B. Losson, Z. Kirkova, M. Rene-Martellet, E. Papadopoulos, R. Farkas, E. Napoli, E. Brianti, C. Tamponi, A. Varcasia, A. Alho, L. Carvalho, L. Cardoso, C. Maia, V. Mircean, A. Mihalca, G. Miro, M. Schnyder, C. Cantacessi, V. Colella, M. Cavalera, M. Latrofa, G. Annoscia, M. Knaus, L. Halos, F. Beugnet & D. Otranto, 2017. Lungworms and gastrointestinal parasites of domestic cats: A European perspective. *International Journal for Parasitology*, 47, 517–528.
- Grandi, G., L. E. Calvi, L. Venco, C. Paratici, C. Genchi, D. Memmi & L. H. Kramer, 2005. Aelurostrongylus abstrusus (cat lungworm) infection in five cats from Italy. Veterinary Parasitology, 134, 177–182.

- Knaus, M., S. T. Chester, J. Rosentel, A. Kühnert & S. Rehbein, 2014. Efficacy of a novel topical combination of fipronil, (S)-methoprene, eprinomectin and praziquantel against larval and adult stages of the cat lungworm *Aelurostrongylus abstrusus*. *Veterinary Parasitology*, 202, 64–68.
- Martin, R. J., A. P. Robertson & A. J. Wolstenholme, 2002. Mode of action of the macrocyclic lactones. In: *Macrocyclic Lactones in Antiparasitic Therapy*, eds J. Vercruysse & R. S. Rew, CABI Publishing, UK, pp. 125–140.
- Shoop, W. & M. Soll, 2002. Ivermectin, abamectin and eprinomectin. In: *Macrocyclic Lactones in Antiparasitic Therapy*, eds J. Vercruysse & R. S. Rew, CABI Publishing, UK, pp. 1–29.
- Singh, P., I. Scott, A. Jacob, V. M. Storillo & W. E. Pomroy, 2018, Pharmacokinetics of abamectin in sheep, goat and deer, *Small Ruminant Research*, 165, 30–33.
- Traversa, D. & A. Di Cesare, 2016. Diagnosis and management of lungworm infections in cats: Cornerstones, dilemmas and new avenues. *Journal of Feline Medicine and Surgery*, **18**, 7–20.
- Traversa, D., S. Morelli, A. Di Cesare & A. Diakou, 2021. Felid cardiopulmonary nematodes: Dilemmas solved and new questions posed. *Pathogens*, **10**, 30.
- Vercruysse, J., P. Holdsworth, T. Letonja, D. Barth, G. Conder, K. Hamamoto & K. Okano, 2001. World Organization for Animal Health. International harmonisation of anthelmintic efficacy guidelines. *Veterinary Parasitology*, **96**, 171–193.
- Vercruysse, J., P. Holdsworth, T. Letonja, G. Conder, K. Hamamoto, K. Okano & S. Rehbein, 2002. International harmonisation of anthelmintic efficacy guidelines (Part 2). Veterinary Parasitology, 103, 277–297.
- Zajac, A. M. & G. A. Conboy, 2012. Veterinary Clinical Parasitology, 8<sup>th</sup> edn, Willey-Blackwell, Ames, Iowa, pp. 5–28.

First study on the efficacy of abamectin in a combined formulation with praziquantel against ....

Zele, D., G. Tavčar-Kalcher, S. Kobal, G. Vengušt, A. Vengušt & I.Grabnar, 2011. Plasma pharmacokinetics of abamectin in fallow deer (*Cervus dama dama*) following subcutaneous administration. *Journal of Veterinary Pharmacology and Therapeutics*, **34**, 455–459.

Paper received 17.09.2021; accepted for publication 19.11.2021

### Correspondence:

Dr. Anton Tonev
Department of Veterinary Microbiology,
Infectious and Parasitic Diseases,
Faculty of Veterinary Medicine,
Trakia University,
6000, Stara Zagora, Bulgaria,
e-mail: 3333tonev@gmail.com