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Case Report

Efficacy and safety of ronidazole treatment against *Tritrichomonas foetus* in a cat colony with multiple disorders

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ABSTRACT

In a group of pedigree cats (n = 17) in poor health condition housed in an animal shelter in Vienna, Austria, with a history of persistent diarrhea, *Tritrichomonas foetus* infection was detected by PCR. Despite pre-existing clinical conditions all cats were treated with ronidazole (30 mg/kg PO q24h for 14 days) under close observation. After treatment, 11 of 14 initially positive animals remained negative for *T. foetus* during the observation period (six to eight weeks post treatment) and no diarrhea was observed. During treatment, nine cats showed mild to moderate neurological disorders (incoordination, mild tremor) at least once; six of these had already shown similar signs before treatment. Ronidazole treatment of multimorbid animals is acceptable if the benefit (here: clinical resolution and release from quarantine for adoption) is high. It is hypothesized that a high degree of inbreeding is a significant risk factor for the development of tritrichomonosis in cats.

1. Introduction

Tritrichomonas foetus (cat genotype) is a protozoan parasite of the large intestine which typically causes chronic intermittent, malodorous, mostly semi-formed large bowel diarrhea in affected cats (Gunn-Moore and Tennant, 2007; Gookin et al., 2017). Although clinical signs may resolve without treatment, it is assumed that untreated cats never fully eliminate the pathogen so that stressful events can lead to recrudescence of the disease (Gookin et al., 2017). Currently, ronidazole is the only drug that has shown sufficient efficacy to eliminate this parasite in the majority of cases (Gookin et al., 2006, 2010; Kather et al., 2007), but the drug is not formally approved for the use in cats. The currently recommended dosage is 30 mg/kg of body weight (BW) per os q24h for 14 days (Gookin et al., 2017). The most important side effect of ronidazole therapy is neurotoxicity in some individuals (Rosado et al., 2007), so treatment is only recommended after a thorough risk-benefit assessment.

Feline *T. foetus* infections in Austria were first published in 2012 (Mostegl et al., 2012), and a study in Austrian catteries revealed an occurrence of 2.5% in single individual samples (Hinney et al., 2015). We here describe the outcome of ronidazole treatment of shelter cats suffering from multiple diseases, including trichomonosis and accompanying neurological conditions.

2. Case presentation

A group of Maine Coon cats was confiscated by the local veterinary officer for welfare reasons in a case of animal hoarding. Animals had been kept in an apartment under crowded conditions with poor welfare and no preventive health care. The colony consisted of 17 intact cats (nine females, eight males) aged from one to six years. They were neutered upon arrival at the public animal shelter and kept under quarantine in individual boxes. Almost all cats showed various clinical conditions, mainly gingivostomatitis, chronical rhinitis and otitis externa. Six cats presented with neurological disorders such as ataxia, head tilt and slight tremor of the head (Table 1). Anamnestically, cases of feline panleukopenia (FPLV) were previously reported in the cat colony. All cats were vaccinated against FPLV after they arrived at the animal shelter (however, this did not provide full protection during the observation period). None of the cats were positive for FeLV/FIV.

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Table 1
Neurological disorders pre- and post-treatment.

Cat No.	Age (years)/sex (f = female, m = male)	Clinical signs pre-treatment	Signs that appeared first during treatment or that were intensified during treatment
2	unknown/f	Mild head tilt, mild head tremor, cause of head tilt not determined	Mild incoordination when jumping
3	4/m	Mild head tilt, moderate ataxia wit incoordination of hind limbs. Cerebellar hypoplasia (likely due to intrauterine parvovirus infection).	Increase of ataxia of hind limbs to moderately severe
4	3/f	Mild head tilt, suspected cause: ear polyps and otitis externa	Mild incoordination when jumping
7	unknown/f	None	Mild head tremor
8	5/m	Mild head tilt, cause of head tilt not determined	Depression; development of mild to moderate head tilt; moderate incoordination of hind limbs
11	2/f	Moderate ataxia with coordination problems on hind limbs and when jumping. Cerebellar hypoplasia (likely due to intrauterine parvovirus infection), ear polyps and purulent otitis externa/ otitis media interna	Depression; extension of moderate incoordination to forelimbs
12	4/m	None	Mild head tremor, mild incoordination when jumping
14	1/m	Moderate ataxia with incoordination of hind limbs and when jumping, moderate head tremor. Cerebellar hypoplasia (likely due to intrauterine parvovirus infection)	None
16	4/m	None	Depression, mild head tremor, mild coordination problems when jumping

As diarrhea occurred in this group of cats which did not resolve after treatment with fenbendazole, three day samples of feces of all cats were examined by coproscopy (flotation), a *Giardia* antigen test (SNAP®, IDEXX GmbH, Ludwigsburg, Germany) and a PCR for the detection of *T. foetus*. After DNA extraction with the ZR fecal DNA MicroPrep™ kit (Zymo Research, Anopoli Biomedical Systems, Eichgraben, Austria) a nested polymerase chain reaction was carried out at the Institute of Parasitology, Vetmeduni Vienna using primers as described by Gookin et al. (2002). Feces were examined no later than one day after collection of the last sample. The first two samples were stored in the fridge prior to examination; the third sample was kept at room temperature.

Fourteen cats were positive for *T. foetus*, seven showed (co)infections with *Giardia* and/or *Cryptosporidium* (Table 2). To exert optimum control over the *T. foetus* infections in this group of cats (and under the assumption that one-time sampling can return false negative results due to intermittent shedding; Gookin et al., 2017) all animals were included in the treatment which was accompanied by a strict hygiene plan. In addition, cats underwent a close health monitoring during the treatment period.

The cats received oral doses of 30 mg/kg BW ronidazole q24 for 14 days in a powder formulation approved for drinking water medication of pigeons (Ridzol® 10%, Dr. Hesse Tierpharma GmbH & Co. KG, Hohenlockstedt, Germany). The product was mixed with water and administered orally with a syringe. When cats did not cooperate the compound was mixed into the wet food and full intake of medication was monitored. Cat No. 4 was inappetent for one day, so one treatment was omitted.

Since *Giardia* infections were diagnosed in the group at the beginning of the study, all cats were additionally treated with 50 mg/kg BW fenbendazole per os (Panacur® MSD Animal Health, Vienna, Austria) q24 for five days. At the end of antiparasitic treatments the whole quarantine unit was disinfected with a two-component disinfectant containing eutectic *o*-hydroxydiphenyl fatty acid and peracetic acid (AscarosterilAB®, KeslaAG, Bitterfeld-Wolfen, Germany).

From the start of treatment until three days afterwards, animals were monitored daily for the early detection of any side effects. Examinations included the assessment of general behavior, body posture, playing behavior, coordination abilities and the general health condition. For the evaluation of coordination, cats were stimulated to follow a laser pointer light. For documentation of these observations a five-point scale (normal, mild, moderate, moderately severe, severe) was used. Primary criteria to interrupt treatment were the occurrence of

Table 2
Parasitological findings and fecal score of cats throughout observation period.

Cat no.	Before treatment			After treatment (wpt: week post treatment)				
	T. foetus	Other protozoa	Fecal score	*T. foetus* 1 wpt	*T. foetus* 3 wpt	*T. foetus* 6–7 wpt	Other protozoa 6–7 wpt	Fecal score 6–7 wpt
1	–	–	1	–	–	–*	–*	1*
2	+	*Cryptosporidium*	**3**	–	–	–**	–	2
3	+	*Giardia*	1	–	–	–	–	1
4	+	–	**3**	–	–	–	–	1
5	+	–	1	–	–	–	–	1
6	+	–	1	–	–	–	–	1
7	+	*Cryptosporidium*	**3**	–	–	–	–	1
8	+	*Giardia*	2	–	–	+**	–	1
9	–	*Giardia*	2	–	–	–	*Giardia*	1
10	+	–	1	–	–	–	–	1
11	+	*Giardia*	1	–	–	+**	–	1
12	+	–	1	–	–	–	–	1
13	+	–	2	–	–	–**	–	2
14	+	*Cryptosporidium*	2	–	–	–**	–	1
15	+	–	1	–	+***	–	–	2
16	+	*Giardia, Cryptosporidium*	1	–	–	–**	*Giardia, Cryptosporidium*	2
17	–	*Cryptosporidium*	1	–	–	–**	–	1

Animals were examined 1, 3 and 6 or 7 weeks (depending on availability of fecal samples) post treatment (wpt = after last administration of ronidazole). – = negative; + = positive * Since no feces were available 6 or 7 wpt, the examination was performed 8 wpt.; ** Follow up examination 8–9 wpt with same results; *** retreated with ronidazole.

severe clinical signs such as anorexia, depression, disorientation or seizures.

The excretion of *T. foetus* after treatment was determined at three time points post examination, one, three and (depending on availability of feces) six to eight weeks post treatment (wpt). Excretion of other parasites and fecal scores were re-evaluated at the final time point. Fecal consistency was scored as fecal score (FS) 1 = firm, 2 = pasty or 3 = semi-liquid (diarrhea).

All cats were negative at the first control examination one wpt, but three shed *T. foetus* at later time points (Table 2). A single treatment cycle with ronidazole suppressed *T. foetus* excretion in 11 out of 14 infected cats for the complete observation period. In one cat the time point of reappearance of *T. foetus* three wpt was linked to surgical intervention (peritoneopericardial hernia), and as this animal did not show neurological disease during first treatment it was retreated. The other two cats were not re-treated as FS were normal and an increase of neurological disorders was observed during first treatment.

Fecal scores improved after treatment in the three cats with diarrhea (FS 3) but the overall occurrence of FS 2 did not change (Table 2).

Ten cats showed clinical signs at least once. In three animals neurological disorders were observed for the first time during treatment (Table 1). In two of them the clinical signs disappeared after treatment was finished, while one cat still had a mild head tremor three days after treatment which ceased thereafter. Of the six cats that presented with neurological signs before treatment one cat showed no change during treatment, while in the other animals a deterioration of the preexisting neurological signs or development of additional clinical signs upon treatment were observed (Table 1, Fig. 1). In the affected cats clinical signs were mild to moderate so treatment was continued. Treatment was also continued in one cat with moderately severe incoordination, as this presented only a slight deterioration of the clinical condition before treatment.

3. Discussion

It is generally recommended not to treat systemically diseased cats with ronidazole (Gookin et al., 2017). In the current case, however, it was assumed that the cats would benefit from treatment because the majority of them presented with chronic diarrhea which precluded them from adoption. They also had to be kept under isolation due to the risk of parasite transmission which was considered to be undesirable beyond a limited duration.

Ronidazole treatment significantly reduced *T. foetus* excretion and diarrhea in the affected cat colony; however, complete elimination of the parasite was not achieved. Similarly, neither ronidazole (which was described as effective against *Giardia* in dogs; Fiechter et al., 2012) nor fenbendazole treatment could completely eliminate *Giardia* infections; two of the five cats that had excreted *Giardia* before the start of treatment still did so at six wpt.

Neither drug is effective against *Cryptosporidium* which was also detected in five animals before and one of them after treatment. This parasite usually causes self-limiting infections, mostly in kittens, which do not usually require treatment in immunocompetent animals (Scorza and Tangtrongsup, 2010). The numerous comorbidities might have contributed to the failure to completely eradicate any of the three protozoa in the highly susceptible animals.

Tolerance and efficacy of ronidazole can be increased by colon-targeted formulations (Reiner et al. 2015; Grellet et al., 2017), which were not available in the present case. Although a guar-gum formulation with pure ronidazole was previously described as superior to Ridzol® 10% (Gookin et al., 2017), in the present study treatment success was comparable to the more concentrated formulation (Grellet et al., 2017) and in line with previous reports (Reinert et al., 2015).

As neurological disorders were already observed before treatment in some of the cats, it is difficult to judge whether any of the clinical signs observed during treatment were directly related to it. In cases where the clinical condition occurred for the first time, it is assumed that this was at least in part caused by the neurotoxic side effects of ronidazole. The affected animals were pedigree cats with a high degree of kinship due to uncontrolled inbreeding. Pedigree cats are frequently described to be at higher risk for infection with *T. foetus* (Gookin et al., 2017). It may thus be hypothesized that a high degree of inbreeding may contribute to genetic disposition for *T. foetus*-infection in cats at least in the present case.

4. Conclusion

Especially under crowded (shelter) conditions, treatment of cats

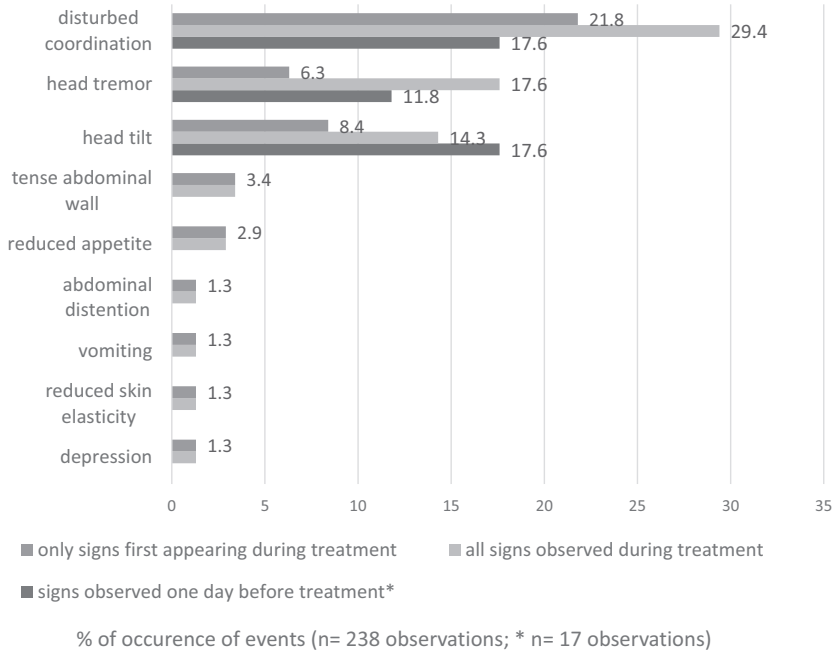

Fig. 1. Frequency of the occurrence of clinical signs during treatment (all signs: signs that were observed during treatment but already occurred pre-treatment).

affected by *T. foetus* is recommended to limit parasite transmission to other animals, and this should not generally exclude multimorbid animals. A prerequisite for treatment safety and efficacy of ronidazole treatment is close health monitoring and implementation of a strict hygiene management during treatment period. Although improvement of diarrhea can be expected upon treatment, complete pathogen elimination may not be feasible in all treated animals. However, this should not preclude shelter cats from adoption when diarrhea is under control.

Ethics statement

This project was discussed and approved by the institutional ethics and animal welfare committee of the University of Veterinary Medicine, Vienna, in accordance with GSP guidelines and national legislation (ETK-02/05/2016).

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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