



VET TALK

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RONIDAZOLE FOR TREATING TRICHOMONAD INFECTIONS IN CATS*

Trichomonads are single-celled, flagellated protozoans that reproduce by binary fission and undergo direct transmission from host to host. The distinctive feature of trichomonads is an undulating membrane that courses the entire length of the organism. *Trichomonas foetus* (TF) is recognized as an important venereal pathogen of naturally bred cattle in which the organism is transmitted from the prepuce of the bull to the vagina and uterus of the cow. The primary clinical manifestation of infection in cattle is infertility, with occasional abortions during the first half of gestation. The organism has also been described as an inhabitant of the porcine gastrointestinal and nasal mucosa, where its pathogenicity is uncertain. Beginning in 1996, several reports have documented the presence of large numbers of trichomonads in fecal samples from young, densely housed cats with chronic large bowel diarrhea. Based on detailed morphologic analysis and sequence identity of rRNA, the feline organisms have been identified as *T. foetus*. Following experimental infection, *T. foetus* colonizes the feline ileum, cecum, and colon and results in diarrhea characteristic of the natural infection.

Signalment, Prevalence and Risk Factors

Naturally occurring *T. foetus* infection is prevalent among young, densely housed cats. Infections are seen in both non-purebred (sheltered) and purebred (cattery) cats, and there is no sex predilection. Gookin and Stebbins determined that the prevalence of *T. foetus*

infection was 31% among 117 purebred cats from 89 cattery owners attending an international cat show. Although there was no relationship between age and the presence of *T. foetus* infection among this group, cats with associated diarrhea are typically young. In one study, approximately 75% of cats were 1 year of age or younger at the time of diagnosis. Catteries in which *T. foetus* was identified had larger numbers of cats with diarrhea and more cats per square foot of cattery space, suggesting that crowding may be a significant risk factor for infection. Proximity of a cattery to agricultural species (pigs, cattle, horses), feeding of raw meat, type of water source, outdoor contact, and history of travel were not identified as significant risk factors for *T. foetus* infection. Coinfection by *T. foetus* and *Giardia* was common. *T. foetus* was not demonstrated by either direct microscopic examination or protozoal culture of feces from 100 feral cats or 20 healthy indoor cats from geographic regions comparable to those of naturally infected cats. Thus, *T. foetus* does not appear to be a component of the normal feline intestinal flora.

Clinical Signs

In domestic cats, *T. foetus* colonizes the colon, resulting in chronic large bowel diarrhea. The diarrhea is characterized by a waxing and waning course and occasionally contains fresh blood and mucus. Diarrhea is semi-formed to cow-pie consistency and is malodorous. In very young cats and with poor

housing conditions, the anus may appear edematous, erythematous, and painful; involuntary dribbling of feces or rectal prolapse may be seen. In general, cats otherwise maintain good health and body condition during infection. A consistent feature of *T. foetus* diarrhea is improved fecal consistency and disappearance of trichomonads during administration of antimicrobial drugs with a return of diarrhea containing trichomonads shortly after drugs are discontinued. Misdiagnosis of *Giardia* is common in cats having *T. foetus* infection. Cats diagnosed with *Giardia* on the basis of direct fecal smear examination that fail to respond to appropriate antimicrobial therapy should be closely reevaluated for the possibility that the observed trophozoites were *T. foetus*.

Diagnosis

Feline *T. foetus* infection is diagnosed by direct fecal smear examination for trichomonads, cultivation of feces using a commercially available system (In

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Pouch TM TF, Biomed Diagnostics, White City OR; www.biomed1.com), or extraction of DNA from feces and amplification of *T. foetus* DNA by polymerase chain reaction (PCR) using species-specific primers.

Treatment

Until recently, an effective antimicrobial treatment for feline *T. foetus* infection had not been identified. Cats infected with *T. foetus* have failed treatment with recommended (and in many cases higher) dosages of numerous antimicrobial drugs, including metronidazole, fenbendazole, albendazole, sulfadimethoxine, trimethoprim-sulfadiazine, furazolidone, tylosin, enrofloxacin, amoxicillin, clindamycin, paromomycin, and erythromycin. Furthermore, *in vitro* studies of feline *T. foetus* in culture have revealed multiple drug resistance (e.g., to paromomycin, furazolidone, metronidazole, neomycin, azithromycin, ciprofloxacin, chloroquine, doxycycline, tinidazole, and clotrimazole). A recent investigation at North Carolina State University College of Veterinary Medicine examined the effect of *in vitro* ronidazole against TF and was reported at the American College of Veterinary Internal Medicine (ACVIM) Forum in Baltimore in May 2005.

Dr. Jody Gookin experimentally infected ten 10-week-old neutered female cats with 3×10^6 TF organisms. All cats became positive for TF infection by culture and developed loose feces by two weeks post infection. Cats were randomized into two groups and treated with placebo (dextrose powder, encapsulated in size #3 gelatin capsules) or ronidazole (encapsulated in empty gelatin capsules) at 10mg/kg orally twice daily for 2 weeks. The ronidazole treatment group initially responded to therapy but relapse infection occurred in all 5 cats receiving ronidazole within 2-20 weeks. None of the cats receiving dextrose responded to therapy, and there was no spontaneous remission reported in either group after 20 weeks. As cats in the ronidazole 10mg/kg treatment group relapsed, they were treated with 30-50mg/kg orally twice daily for 2 weeks past therapy.

After 20 weeks of infection, the placebo group was also treated with 30-50mg/kg orally twice daily for 2 weeks. At the end of the study, 9/10 cats in both groups had been cleared of the TF. Throughout the study period, no clinicopathological abnormalities or adverse effects were noted. The researchers therefore concluded that ronidazole administered at 30-50mg/kg orally twice daily for 2 weeks is capable of resolving diarrhea and eradicating infections of TF in cats.

Clinical use of ronidazole in cats following Dr. Gookin's study has revealed that some cats will exhibit reversible neurological toxicity from ronidazole. While this adverse effect has mostly been observed in cats at the 50mg/kg dose, it is possible in all dosage ranges, and cats should be monitored for any signs of nystagmus, ataxia and behavior change. Ronidazole should be discontinued immediately in cats exhibiting these signs. Ronidazole toxicity is similar to that seen with metronidazole toxicity and in addition to supportive therapy and discontinuation of drug, competitive inhibition at the GABA receptor by diazepam may also prove therapeutically beneficial. It is interesting to note that Dr. Gookin has also recently been awarded a grant to examine the use of tinidazole in cats infected with TF. Results from that study are forthcoming.

Ronidazole is available as water-soluble powders for treatment of canker under a number of brand names worldwide, including Ridsol-S®, Turbosole®, Tricho-Plus®, and Ronivet®; however, ronidazole is not approved for veterinary use in the United States. The usual strength of commercial products is 10% ronidazole in powder for addition to drinking water. The drug is very bitter and preparations stronger than 10% tend to be unpalatable. While these 10% powders are available from veterinary distributors through the internet, the 10% concentration renders them relatively useless in treating cats. Specifically, at 30-50mg/kg orally twice daily, a 5kg cat would require 150mg – 250mg of ronidazole or 1.5g to 2.5g of the powder twice daily. It is unlikely that any

client could successfully administer these large volumes of unpalatable powder twice daily for the required 2 weeks of therapy. For this reason, many compounding pharmacists have begun stocking pure ronidazole powder, similar to that used in Dr. Gookin's study, to be compounded into individual doses for cats affected with TF pursuant to a veterinarian's prescription for an individual animal. Doses of ronidazole are usually prepared by compounding pharmacists as capsules containing the exact dose as prescribed. Capsules of ronidazole are the most desirable dosage form for several reasons. Capsules mask the extremely bitter taste of ronidazole; exact dosing reduces risk of neurotoxicity that has been reported at higher doses; and the owner can be assured that the entire dose was ingested after administration of a capsule. Stability of ronidazole in aqueous solutions is apparently not longer than 24 hours, as manufacturers recommend that fresh solutions be made daily if ronidazole powder is added to water. Chewable treats containing prescribed doses may also be compounded, but the bitter taste of ronidazole may be difficult to mask, and ronidazole treats would have to be stored at -20°F as recommended by chemical suppliers. As ronidazole is a potential carcinogen, veterinarians prescribing ronidazole should practice informed consent with cat owners, and recommend that caregivers wear gloves while administering the drug and while cleaning the litter box. Feces should be double bagged and disposed of in the regular trash to avoid contamination of watersheds and landfills. Ronidazole is banned for use in food-producing animals due to the carcinogenic potential to humans.

(References available upon request.)

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