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Efficiency of Antihelmitic Drugs in The Treatment of Canine Intestinal Nematodes

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Abstract

The work presents the effectiveness of anthelmintic drugs in the treatment of canine intestinal nematodoses, since gastrointestinal parasites are the most common canine infectious agents and cause developmental delay, anorexia, anemia, diarrhea, which leads to significant damage to the dog's body and even death. In this regard, the analysis of the comparative efficacy of anthelmintic drugs for nematodoses in naturally invasive dogs was the aim of the present studies. As a result, it was found that using the combined therapeutic scheme of anthelmintic and probiotic, the complete disappearance of canine helminthiasis clinical signs was noted by the 10th day of treatment. This indicates a positive effect of symptomatic therapy for helminthiases.

Keywords: canine, nemotodoses, anthelmintics, treatment, efficiency, probiotics.

INTRODUCTION

Among the many stereotypes of symbiosis in ecosystems (commensalism, mutualism, protocooperation, etc.) parasitism is a type of negative interpopulation interaction, when one population unilaterally uses another, causing it certain harm [1]. The biological optimum of the flow of life processes in the organism of animals, realized through the normal course of physiological processes, can easily be disrupted due to the pathology of a contagious and non-contagious etiology [2, 4]. The development of these disorders is possible at any age and in any living organisms [4].

Gastrointestinal parasites are the most common infectious agents in dogs. They cause developmental delay, anorexia, anemia, diarrhea, which leads to significant damage to the dog's body and even death, especially in young or old animals and animals with reduced immunity [5, 6]. Extensiveness of dog invasion reaches 82% according to A.N. Volicheva, V.V. Gorokhova. A number of researchers believe that invasion occurs in puppies up to 100% [7, 8]. In this regard, special attention is paid to nematodes because of the high pathogenicity characteristic of both the puberty intestinal stage in dogs and tissue larval forms that can affect a wide range of animals and humans [9-11].

The spread of nematodes is due to the accumulation of a large number of domestic dogs, the use of ineffective drugs or with violation of therapeutic regimens [6], along with a lack of awareness of the owners and the lack of adequate sanitary measures [12-14]. It should be noted that deworming helps not only to release animals from worms, but also to reduce environmental pollution [15-18]. Moreover, the success of the activities depends on the effectiveness of anthelmintic drugs with targeted effects on a particular type of pathogen [10, 19]. In this regard, the search for anthelminthics and the possibility of their effective use is of great interest for veterinary science and practice.

The spread of nematodoses is due to the accumulation of a large number of domestic dogs, the use of ineffective drugs or with violation of therapeutic regimens [6], along with a lack of awareness of the owners and the lack of adequate sanitary measures [12-14]. It should be noted that deworming helps not only to release animals from worms, but also to reduce environmental pollution [15-18]. Moreover, the success of the activities depends on the effectiveness of anthelmintic drugs with targeted effects on a particular type of pathogen [10, 19]. In this regard, the search for anthelminthic drugs and the possibility of their effective use is of great interest for veterinary science and practice.

The aim of the study is to analyze the comparative effectiveness of anthelmintic drugs for nematodoses in naturally invasive dogs.

MATERIALS AND METHODS

The study was performed on dogs (n=22), affected by helminthiasisю They were diagnosed by the Kotelnikov-Khrenov helminthic method.

Microscopic studies were performed on a biological microscope (MBI). The determination of the detected helminth eggs was performed using determinants and monographs of K.I. Scriabin and A.M. Petrova (1964), K.I. Abuladze (1964), used the "Atlas of differential diagnosis of helminth infections on the morphological structure of eggs and larvae of pathogens" A.A. Cherepanova (2001) [21-22].

To determine the therapeutic efficacy of therapy for our work, we chose two drugs - Milprazon® tablets for dogs, developed by KRKA, dd, Novo mesto, Slovenia and Drontal plus, developed by Woweg Animal Health GmbH. The choice was made taking into account information on therapeutic activity, the spectrum of action on nematodes of dogs and availability in veterinary pharmacies in Russia. To evaluate the anthelmintic drugs, animals were given based on 1 kg of body weight and individually in tablet form according to the manufacturer's instructions (Tables 1, 2). One time in the morning. A hungry diet according to the instructions of these drugs was not required.

In the study, animals from the control and experimental groups were selected on the principle of analogs, taking into account the breed, age, sex, live weight and species composition of helminths. All animals were in the same conditions of feeding and housing and were domestic dogs.

Group 1 - the control, not infected helminthism dogs, 5 heads.

Group 2 - 4 dogs infected with T.leonina, age from 1.6 to 5 years, received Milprazon tablet for dogs.

Group 3 - 4 dogs infected with T.leonina, age 2 to 7 years, received the drug Drontal Plus.

Group 4 - puppies and young dogs with T. canis infestation, age from 5 months to 1.1 years, 5 heads. They received the drug Milprazon tablets for dogs + probiotic Laktobifadol for dogs at a dosage of 0.2 g per 1 kg of body weight 2 times a day for 10 days (according to instructions). Group 5 - 4 young dogs with T. canis invasion, age from 1 year to 1.8, received treatment with Drontal plus + probiotic Laktobifadol for dogs in a dosage of 0.2 g per 1 kg of weight 2 times a day for 10 days (according to instructions).

The study of the dogs' feces of the experimental groups was carried out on the 10th and 20th days after giving antihelminth drugs.

Table 1 – Doses of Milprazon tablets for dogs

Milprazon tablets for dogs		
Body weight, kg	Tablets for puppies and dogs with a live weight up to 5 kg (milbemycin oxime - 2,5 mg and praziquantel - 25 mg), pcs	Tablets for puppies and dogs weighing more than 5 kg (milbemycin oxime - 12,5 mg и praziquantel -125 mg), pcs
0,5-1	1/2	
1-5	1	
5-10	2	1
10-25		1
25-50		2
50-75		3

Table 2 – Doses of Drontal plus tablets for dogs

Body weight, kg	Drontal plus dose, tabs
Puppies and small breed dogs	
2-5	1/2
6-10	1
Medium breed dogs	
11-20	2
21-30	3
Large breed dogs	
31-40	4
41-50	5

After establishing the efficacy of the drugs, Milprazon tablets were used for dogs in the veterinary clinic for 2 dogs with invasion by nematodes of this family. Ancylostomatidae, age from 1.4 years to 5 years, 2 dogs with combined invasion of T. canis and T.leonina and one dog with T. vulpis invasion at the age of 3 years. All animals received Milprazon tablets for dogs with the addition of probiotic Laktobifadol for dogs at a dosage of 0.2 g per 1 kg of body weight 2 times a day for 10 days (according to instructions). Statistical processing of the results was performed using the MedCalc program for Windows.

RESULTS AND DISCUSSION

The pathogenesis of parasitic diseases is very diverse, but generally, it is always characterized by the presence of a large number of divergences and "vicious loops", which is accompanied by an abundance of complications and various forms of pathology, the presence of pathological processes and conditions. These manifestations are very versatile. On the other hand, the presence in the body of the pathological process is conducive to the occurrence of parasitic diseases and serves as one of the most important pathogenetic mechanisms causing the manifestation of the disease [23-26]. As a result, the formation of an algorithm for therapeutic measures is an important component of antihelminthic measures. So, before treatment, in dogs infected with T.leonina, the intensity of egg release was 42.1 ± 2.5 ind./g feces in the second experimental group and 57.0 ± 8.0 ind./g feces in the third. In dogs 4 and 5 of the experimental groups, the intensity of excretion of nematode eggs T. canis was 88.6 ± 3.0 ind./g feces and 83.4 ± 4.0 ind./g feces, respectively (Table 3, 4).

As can be seen from table 3, Milprazon tablets for dogs showed 100% effectiveness in both T.leonina invasion and T.canis invasion, the development cycle of which in the dog's body is one of the most difficult. Already on the 10th day after the treatment, the animals were completely free from the nematode T.leonina. The release from T. canis occurred completely only on the 20th day after giving the anthelmintic drug. On the 10th day, a decrease in the intensity of egg release to 4.5 ± 1.5 ind. / G of faeces was observed (Table 3).

It should be noted that there are no worms were detected in feces of the control group during the entire study. The results of the study Drontal plus showed its 100% effectiveness in invasion by the nematode T.leonina. On the 10th day, the intensity of egg release was obtained 5.0 ± 3.0 ind./g feces, and on the 20th day, the intestines of the dogs were completely released from these nematodes. In dogs invaded by T. canis, Drontal plus showed only 75% efficacy. It can be assumed that this is due to the complex cycle of development of toxocara in the organism of dogs and the ability of their larvae to remain in the tissues, resuming their migration under adverse factors affecting the organism of animals (Table 4).

Table 3 – The results of the study of the effectiveness of the drug Milprazon tablets for dogs

Animal groups	The average number of helminth eggs in 1 g of feces			Efficiency, %
	Before treatment	On the 10^{th} day	On the 20^{th} day	
1, control	-	-	-	-
2, T.leonina invasion	42.1±2.5	-	-	100
4, T. canis invasion	88.6±3.0	4.5±1.5	-	100

Table 4 – The results of the study of the effectiveness of the drug Drontal plus

Animal groups	The average number of helminth eggs in 1 g of feces			Efficiency, %
	Before treatment	On the 10^{th} day	On the 20^{th} day	
1, control	-	-	-	-
3, T.leonina invasion	57.0±8.0	5.0±3.0	-	100
5, T. canis invasion	83.4±4.0	6.5±2.5	1.0±1.0	75

Table 5 – The results of the study of the effectiveness of the drug Milprazon tablets for dogs

Nematode kind	The average number of helminth eggs in 1 g of feces			Efficiency, %
	Before treatment	On the 10^{th} day	On the 20^{th} day	
Ancylostomatidae	28.1±2.0	2.4±1.0	-	100
concomitant invasion T. canis and T.leonina	61.0±6.0 36.5±3.5	1.5±0.5 -	- -	100
Trihuris vulpis	64.5±8.5	4.5±1.5	-	100

The owners of most of the animals studied turned to a veterinary clinic with suspicion of helminthiasis in their pets, which manifested itself in such clinical manifestations as: anorexia, weight loss, dullness and ruffled coat, change in stool consistency (softening), impurities of mucus, and blood. When observing animals in the course of treatment, no side effects and complications of the gastrointestinal tract were noted. By the 20th day of treatment, the condition of the dogs of the experimental groups had improved, the clinical signs of the disease with which their owners had initially applied had disappeared. When using the combined therapeutic regimen of anthelmintic and probiotic, the improvement of the condition was noted by the 10th day of

treatment. Also, by the 10th day, the complete disappearance of the clinical signs of helminthiasis in dogs of the fifth experimental group, infested with T.canis, whose treatment did not give a 100% effective result, was noted. This indicates a positive effect of symptomatic therapy for helminthiases.

The canine drug Milprazon tablets with addition of probiotic Laktobifadol for dogs used in the veterinary clinic. The results of the study are shown in Table 5. As can be seen from the table, clinical trials showed a 100% effective result. The improvement of animals' clinical condition was evident by the 10th day after treatment.

It is important to note that in 2 domestic dogs an invasion was registered by nematodes of the Ancylostomatidae family, which are hematophagous and cause serious damage to the mucous membrane of the gastrointestinal tract and, as a result, chronic drip bleeding and inflammation of the small intestine. Inclusion of probiotic into the therapeutic regimen of these animals also improved their clinical condition by the 10th day. This improvement is impossible to achieve with the use of a single anthelmintic drug.

Our data are consistent with the conclusions of other authors. Parasitosis is a common definition for infectious diseases of all groups (infections, mycoses, invasions, infestations), if their pathogens are parasites of a susceptible host, form with it a stable parasitic system with a level of interaction of the population + population of susceptible animals. Since, on the basis of the principle of biological recognition, the stability of the parasitic system is proportional to its specificity, pathogenic parasites are mostly monohostal and monopathogenic [16, 27].

The main means of control animal parasites is the use of effective anthelmintics. Means used in the form of tablets for oral use are convenient to use by dog owners. Milprazon tablets for dogs with the taste of meat, which facilitates the giving of the drug. As an active ingredient Milprazon tablets for dogs contain milbemycin oxime and praziquantel. Milbemycin oxime is an effective modern drug for nematodes that does not have parasite resistance.

Milbemycin oxime is a macrocyclic lactone resulting from the enzymatic activity of Streptomyces hygroscopicus var. Aureolacrimosus, active against larvae and imago nematodes parasitizing in the gastrointestinal tract of dogs. The mechanism of action of milbemycin is due to an increase in the permeability of cell membranes to chlorine ions, which leads to overpolarization of the cell membranes of the nervous and muscular tissue, paralysis and death of the parasite. The maximum concentration of milbemycin oxime in the blood plasma of dogs is achieved within 2-4 hours, the bioavailability is about 80%. From the body, the compound is excreted mostly unchanged.

In our work, Milprazon canine tablets howed 100% effectiveness in both T.leonina invasion and T. canis invasion, the development cycle of which in the dog's body is one of the most difficult. Already on the 10th day after the treatment, the animals were completely free from the nematode T.leonina. The release from T. canis occurred completely only on the 20th day after giving the anthelmintic drug.

The results of the study Drontal plus showed its 100% effectiveness in invasion by the nematode T.leonina. On the 20th day there was a complete release of the intestines of dogs from these nematodes. But with the invasion of T. canis, Drontal plus showed an efficiency of only 75%. It can be assumed that this is due to the complex cycle of development of toxocar in the organism of dogs and the ability of their larvae to remain in the tissues, resuming their migration under adverse factors affecting the organism of animals.

Drontal Plus contains in its composition Pyrantel Embonate and Febantel - active substances against nematodes. The authors in experiments to determine the effectiveness of these substances in the invasion of T. canis recommend a minimum of two times the use of [16, 18, 28] or multiple administration [29], and the effectiveness was not noted in all cases. Therefore, a single use, as indicated in the instructions of Drontal plus, is not enough for dogs toxocariasis. Most often, liver damage in animals is found when anti-bacterial, anti-tumor and antiparasitic drugs are prescribed [30, 31]. Along with this, it is known that one of the negative effects of helminths on the host organism is the development of vitamin and trace element deficiencies and the study of this trend is relevant [31]. The combined effect of vitamin preparations is synergistic, and has additive, antagonistic nature of the interaction [32]. There are works, which aimed at correcting the hepatotoxic effect of anthelmintic drugs on animals with pharmacological agents. Variants of joint use of drugs with antiparasitic macrocyclic lactones widely used in veterinary practice are being tested now [30, 31, 33].

The negative effects of parasitosis on the host's immune system have been proven, but negative side effects of most anthelmintic drugs have also been identified [34, 35]. In this regard, the therapy of helminth infections can be ineffective, in itself, cause additional stress on the immune system and lead to the development of immunodeficiency states in combination with pathological processes provoked by helminths. Conducting a combination therapy of helminthiasis, based on the combined use of specific treatments and immunomodulatory drugs as additional, will improve the effectiveness of treatment and prevent complications.

In our work, we choose for the combined use of the anthelmintic drug and probiotic. The drug Laktobifadol is intended for the treatment and prevention of dysbiosis, diarrhea, improve digestion. During pregnancy to obtain a healthy offspring and in the postpartum period for the normalization of lactation. Puppies and kittens in the first 30 days of life, as well as animals older than 5-7 years for the prevention of age-related dysbiosis. With the pathology of the stomach, intestines, liver, pancreas and kidneys. For improvement of a metabolism, immunity, a condition of skin and wool. In some forms of dermatitis. And also according to the instructions of the drug it is used after deworming.

In our work, we noted that when using the combined therapeutic scheme of anthelmintic and probiotic, the improvement of the state was noted by the 10th day of treatment. Due to the fact that the owners of most of the animals studied turned to a veterinary clinic with suspicion of helminthiasis in their pets, which manifested itself in such clinical manifestations as: deterioration of appetite, weight loss, dullness and ruffled coat, change in stool consistency (softening), impurities mucus, blood, we were able to track changes in the clinical condition of dogs. When probiotics were included in the therapeutic treatment regimen for animals, an improvement in their clinical condition was noted by the 10th day. This improvement can not be achieved by using only one anthelmintic drug. By the 10th day of complex treatment, the complete disappearance of the clinical signs of helminthiasis in dogs of the fifth experimental group invaded by T. canis was noted, whose treatment did not give a 100% effective result in monotherapy with an anthelmintic drug. This indicates a positive effect of symptomatic therapy for helminthiases.

CONCLUSION

The anthelmintic drug Milprazon canine tablets in the experiment showed 100% efficacy in the invasion of T.leonina and T.canis. On the 10th day after the treatment, the animals were completely free from the nematode T.leonina. Exemption from T.canis occurred completely on the 20th day after giving the anthelmintic drug. The results of the study Drontal plus showed its 100% effectiveness in invasion by the nematode T.leonina (full release on the 20th day). With T. canis invasion, Drontal plus showed only 75% effectiveness. When using the combined

therapeutic regimen of anthelmintic and probiotics, the complete disappearance of the clinical signs of helminthiasis in dogs was noted by the 10th day of treatment. This indicates a positive effect of symptomatic therapy for helminthiases. Clinical trials showed a 100% effective result of Milprazon tablets for dogs with pathogens such as: nematodes from Ancylostomatidae, T.canis, T.leonina, T.vulpis. When probiotics were included in the therapeutic treatment regimen of these animals, their clinical condition improved already by the 10th day.

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