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Therapeutic efficacy of the drug Simparica® for demodicosis in dogs in the Kamianets-Podilskyi, Ukraine

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Abstract

The purpose of our research was to test the therapeutic efficacy of the acaricide «Simparica®» in combination with the biostimulator «Catosal» and the hepatoprotector «Tioprotectin» for demodicosis in dogs in the conditions of veterinary clinics in the Kamianets-Podilskyi, Ukraine. The study has been performed on dogs of different genders, ages and breeds that had a generalized form of demodicosis (affected at least 6 areas on the body of animals), to test the effectiveness of this drug in different treatment schemes. Acarological studies of scrapings from the skin of experimental animals for the presence of live or dead mites Demodex canis or their eggs have been carried out by the vital method according to D.O. Pryselkova. As a result of the conducted researches the choice of acaricidal drugs and development of complex therapeutic measures for demodicosis of dogs has been experimentally substantiated. The drug «Simparica®» has proved to be quite effective against demodicosis of dogs, even with a single use. The dependence of the effectiveness of the use of prolonged acaricide «Simparica®» on clinical forms of demodicosis has been shown. The absolute therapeutic effect of acaricide is obtained in the scaly form of demodicosis. However, in pustular and mixed clinical forms of demodicosis, its effectiveness decreased to 71.4 and 57.1%, respectively. In combination with the drug of pathogenetic therapy «Catosal» for pustular and mixed forms of demodicosis, the therapeutic efficacy of the drug «Simparica®» increases to 85.7%. When added to the scheme of hepatoprotector "Thioprotectin", it is possible to achieve 100% therapeutic effect in pustular forms of demodicosis. However, in severe mixed form of demodicosis, the effectiveness was not absolute and was only 85.7%. In case of generalized demodicosis of dogs, regardless of clinical forms, it is recommended to use the acaricide «Simparica®» in combination with the drug «Catosal» and in the combination of «Catosal» and «Thioprotectin».

Keywords: Dogs; Demodicosis; «Simparica®»; «Catosal»; «Thioprotectin»

1. Introduction

In the etiology of dog skin diseases dermatitis of parasitic origin is registered quite often, due to their significant share in the structure of skin diseases, relatively low effectiveness of treatment, ecology of large cities and a number of other factors [1, 2]. Urban dog populations are intensively affected by negative factors, including high stress, unsatisfactory environmental situation, feeding with dry and other concentrated feeds, uncontrolled breeding, etc., which contributes to the emergence and spread of animal skin diseases, including demodicosis [3, 4, 5].

At present, it has been established that demodicosis invasion in dogs has a very diverse clinical manifestation – from localized to complicated generalized dermatitis of various kinds with damage to internal organs [6].

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Therefore, given the abovementioned, it is important to carry out timely (early) diagnosis of demodicosis, followed by the use of specific most effective acaricides-drugs and means to mobilize the protective properties of the animal. Meanwhile, the development and implementation of new effective acaricides for the treatment of demodicosis of the dog and the study of their effectiveness in various forms of the invasion remain relevant.

It is known that the complexity of chemotherapy for demodicosis is its tendency to damage not only the skin but also internal organs. Therefore, external application of acaricides is not always effective, especially in the generalized process [7, 8]. Virtually all acaricides of systemic action, including ivermectins and some pyrethroids, have an acaricidal effect on adult mite, but preimaginal stages, which are in a passive state, do not die because they do not feed. With the onset of favourable conditions (cessation of treatments) larvae and nymphs become active, turn into adults and the number of mites quickly recovers [9]. In this regard, there is a search for long-acting drugs that would create a concentration of the active substance in the body for a long time, which would allow to achieve the absolute therapeutic effect of demodicosis [8, 10]. One such modern remedy is the acaricide «Simparica®».

The purpose of our research was to test the therapeutic efficacy of the acaricide «Simparica®» in combination with the biostimulator «Catosal» and the hepatoprotector «Tioprotectin» for demodicosis in dogs in the conditions of veterinary clinics in the Kamianets-Podilskyi, Ukraine.

2. Material and methods

Experimental studies have been conducted at the Department of Infectious and Parasitic Diseases in Higher Educational Institution «Podillia State University», Kamianets-Podilskyi, Ukraine. During 2021, a series of experiments to determine the therapeutic efficacy of modern drug «Simparica®» was performed on dogs spontaneously affected by demodex. The study was performed on dogs of different genders, ages and breeds that had a generalized form of demodicosis (affected at least 6 areas on the body of animals), to test the effectiveness of this tool in different treatment schemes. The scheme of experiment is shown in Table 1.

Table 1 Scheme of experiment

Clinical form of demodicosis	Groups of animals	Treatment scheme
Scaly	I (control)	«Simparica®» – individually, orally with food, at a dose of 4 mg ADR (sarolaner)/kg body weight, once
Pustular		
Mixed		
Scaly	II (experiment)	«Simparica®» – similar to the first group. «Catosal» – intravenously, once a day at a dose of 3 ml for 5 days
Pustular		
Mixed		
Scaly	III (experiment)	«Simparica®», «Catosal» – similar to the first and second groups. «Thioprotectin» – intravenously, once a day at a dose of 3 ml for 5 days
Pustular		
Mixed		

A control and two experimental groups of dogs have been formed to conduct the study. Each group included animals with generalized scaly, pustular, and mixed forms of demodicosis.

Mostly dogs of both genders older than 12 months with a body weight of 5-15 kg were included. With the exception of clinical signs of generalized demodicosis, the dogs were healthy and did not receive corticosteroids or any drugs that had an acaricidal effect for at least 1 month before inclusion in the study. As a preventive measure, 14 days before the experiment, all experimental dogs received subcutaneous antibiotic Amoxicillin at a rate of 1 ml per 10 kg of animal weight (15 mg of Amoxicillin per kg of body weight) for 5 days with an interval of 24 hours. A positive result of deep skin scraping on Demodex canis from five areas of each animal was used as a mandatory criterion for the inclusion of dogs in the experiment.

Animals in the control group used a prolonged systemic insecticide of new generation «Simparica®» (Zoetis Inc, USA). The active substance of the drug is sarolaner, which belongs to the group of isoxazolines, has acaricidal and insecticidal activity. Sarolaner blocks GABA-dependent and glutamate receptors of the nervous system of ectoparasites, which disrupts the absorption of chlorine ions by these receptors. This leads to damage to the nervous system of ectoparasites and their death. This action is characteristic only of invertebrates and is safe for mammals.

In the second research group, in addition to «Simparica®», was used «Catosal» (Bayer HealthCare LLC, USA). «Catosal» – a complex drug containing in 100 ml: butaphosphan (10 g), cyanocobalamin (0.005 g), methyl 4-hydroxybenzoate (0.1 g), and water for injections. The drug has tonic properties, normalizes metabolic and regenerative processes, has a stimulating effect on protein, carbohydrate and fat metabolism, increases the body's resistance to adverse environmental factors.

Animals of the third experimental group in addition to the above drugs obtained hepatoprotector «Thioprotectin» (Arterium, Ukraine). The active substance of the drug is thiotriazolin. The pharmacological effect of the drug is due to antioxidant, membrane stabilizing and immunomodulatory properties. The drug prevents hepatocyte death, reduces the degree of fatty infiltration and the spread of centrilobular necrosis of the liver, promotes reparative regeneration of hepatocytes, normalizes protein, carbohydrate, lipid and pigment metabolism, increases the rate of synthesis and secretion of bile, normalizes the composition and secretion of bile. «Thioprotectin» enhances the compensatory activation of anaerobic glycolysis and activates oxidation processes in the Krebs cycle while preserving the intracellular ATP fund, improves the rheological properties of blood by activating the fibrinolytic blood system. All drugs were used according to the instructions for their use.

During the experiment, the number of mites in the taken samples was counted, and the severity of demodicosis foci in each dog was assessed before treatment and for 2 months of the study with an interval of 20 days. Each subsequent examination included taking a deep scraping of the skin (~5 cm^2) on the same five parts of the animal's body. When taking the material, the method of deep (before the appearance of blood) scrapings of the skin was used for the study on the border of the affected and healthy skin from at least 3-4 places. Acarological studies of scrapings from the skin of experimental animals for the presence of live or dead mites Demodex canis or their eggs have been carried out by the vital method according to D.O. Pryselkova. The evaluation criterion was the indicator of extenseffectiveness of drugs [10, 17].

Statistical processing of the results has been performed by methods of variation statistics using the program Statistica 9.0 (StatSoft Inc., USA).

3. Results

It is known that during demodicosis there are deviations in the functioning of the immune system as a result of intoxication of the body by the products of mite activity, decay of its own tissues and severe immune inflammation affects the liver. Therefore, hepatoprotector «Thioprotectin» and biostimulator «Catosal» have been included in the treatment of demodicosis in dogs. The results of experiment are shown in Table 2.

Table 2 Intensity of recovery of dogs with generalized demodicosis when using «Simparica®» individually and in combination therapy

Clinical form of demodicosis	Groups of animals											
	I (control)				II (experiment)				III (experiment)			
	Total, n	Recovered (absence of live mites), n			Total, n	Recovered (absence of live mites), n			Total, n	Recovered (absence of live mites), n		
		on the 20th day	on the 40th day	on the 60th day		on the 20th day	on the 40th day	on the 60th day		on the 20th day	on the 40th day	on the 60th day
Scaly	12	-	5	7	13	3	6	4	11	4	5	2
Pustular	9	-	2	4	12	-	4	5	14	2	5	6
Mixed	7	-	2	2	11	-	4	5	12	1	4	5
Total in group	28	-	9	13	36	3	14	14	37	7	14	13

Footnote: n - number of animals.

When using the acaricide «Simparica®» on the 20th day of the experiment in all clinical forms of demodicosis, single live mites were found in the scrapings in the field of view of the microscope. On the 40th day of the experiment in five animals with scaly form and two animals with pustular and mixed forms of demodicosis live mites were not found, and on the 60th day of the experiment – in the scaly form all the animals recovered, in the pustular and mixed form three animals remained sick.

In the animals of the 2nd experimental group, which in addition to «Simparica®» received a biostimulator «Catosal», the dynamics of recovery was more intense and on the 40th day of the experiment nine animals with generalized scaly form of demodicosis and four animals with pustular and mixed forms of demodicosis completely freed from live mites. On the 60th day of the experiment live mites were not found with scaly generalized form in scrapings from all animals, and single live mites were found with pustular and mixed forms, respectively, in three and two samples.

The best dynamics of recovery was obtained with the use of complex therapy in the composition of prolonged acaricide «Simparica®», stimulator «Catosal» and hepatoprotector «Thioprotectin» (3rd experimental group) according to the standard method of application. At the same time, on the 40th day, in the scaly form, nine animals were completely freed from demodex, in the pustular and mixed forms – seven and five animals, respectively. On the 60th day of the experiment in this group of animals in the generalized scaly form of demodicosis, all selected samples did not contain live mites, and in pustular and mixed forms, respectively, in one and two experimental samples were found single specimens of live mites *Demodex ca*nis.

In determining the therapeutic efficacy of the used treatment schemes, animals with a generalized form of invasion were deliberately taken into the experiment. It is known that in this course, the treatment of demodicosis is problematic. As a result of the experiment, the effectiveness of the used schemes of therapy for demodicosis of dogs was different (Table 3).

Table 3 Therapeutic efficacy of experimental treatment schemes at demodicosis of dogs with generalized invasion

Clinical form of demodicosis	Groups of animals					
	I (control)		II (experimental)		III (experimental)	
	Total animals	Recovered	Total animals	Recovered	Total animals	Recovered
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Scaly	12 (100)	12 (100)	13 (100)	13 (100)	11 (100)	11 (100)
Pustular	9 (100)	6 (66.7)	12 (100)	9 (75.0)	14 (100)	13 (92.9)
Mixed	7 (100)	4 (57.1)	11 (100)	9 (81.8)	12 (100)	10 (83.3)
Total in group	28 (100)	22 (78.6)	36 (100)	31 (86.1)	37 (100)	34 (91.9)

In particular, in the scaly form of demodicosis invasion of dogs, despite its generalized nature, the used treatment schemes were absolutely effective. Although the dynamics of recovery was much faster than the combined use of acaricide «Simparica®» with «Catosal» and «Thioprotectin».

In the pustular form of demodicosis, the independent use of «Simparica®» in the 1st experimental group did not cure all animals. The effectiveness of therapy was only 66.7%. However, the addition of the drug «Catosal» allowed to increase this figure to 75.0%, and in combination therapy with the drugs «Catosal» and «Thioprotectin» – up to 92.9%.

The most difficult was to treat mixed generalized form of demodicosis in dogs. With the independent use of the drug «Simparica®» in the 1st experimental group, its therapeutic efficacy was only 57.1%. With the use of complex therapy in the 2nd and 3rd experimental groups, the therapeutic efficacy increased to 81.8% and 83.3%, respectively, but was not absolute.

4. Discussion

For the treatment of patients with acarosis of animals, a significant number of drugs based on various chemical compounds have been proposed [3, 8, 11, 12]. However, most of these drugs have certain disadvantages. Thus, organochlorine compounds accumulate in the body and can cause animal poisoning, as well as have embryotoxic and

teratogenic effects. Drugs of the macrocyclic lactone group cause vomiting and short-term anorexia in animals, as well as immunosuppressive effects [13].

Analysis of literature data and own research confirms that demodicosis is a systemic disease of the body. Therefore, it is important to use systemic prolonged acaricides along with pathogenetic and stimulant therapies. This is due to the fact that, localized deep in the skin, mites, especially in encapsulated colonies, are almost invulnerable, because the capsule surrounding the colony is a powerful barrier to acaricides contact action. After the death of the adult, immature forms of *Demodex canis* have a nutrient deficiency, and, feeling its lack, they stop their development and go into a passive state. However, as soon as favourable conditions occur for them (cessation of treatment of a sick animal), larvae and nymphs become active, which leads to the restoration of the colony. This is an important biological specie *Demodex canis*, which not only explains the difficulties of therapy, but also theoretically argues the development of ways and means to combat it [14, 15].

Clinical trials of «Simparica®» have shown its absolute effectiveness only in the scaly form of generalized demodicosis. A natural tendency of dependence of the drug's effectiveness on the severity of demodicosis has been revealed. Therefore, in the mixed generalized form of demodicosis, its effectiveness was only 57.1% [16].

Researchers found found significant changes in morphological and biochemical parameters of the blood in the generalized form of demodicosis in dogs, which indicate functional disorders in the liver and kidneys. Meanwhile, 2.5 months after treatment, morphological and biochemical parameters of the blood probably stabilized and acquired physiological parameters [17, 18].

Based on the literature data and the results of our own research, we can conclude that the nature of changes in biochemical tests for localized and generalized forms of demodicosis in dogs suggests that liver pathology is quite common and can be considered a factor that reduces protective functions of the body.

The presence of liver failure confirms the need to include hepatoprotectors in the treatment of demodicosis [12, 13]. According to research by scientists, the clinical manifestation of demodicosis, in addition to the direct impact of mites on dogs, causes immunodeficiency and reduced resistance of animals [16].

For this reason, we proposed combined schemes of treatment that included «Catosal» (2nd experimental group) and «Catosal» in combination with «Thioprotectin» (3rd experimental group) in addition to the acaricide «Simparica®».

The introduction of the drug «Catosal» into the treatment scheme allowed the 2nd experimental group of dogs to increase the therapeutic efficacy to 86.1%. In the 3rd experimental group, which used hepatoprotector "Thioprotectin", in addition to the mentioned drugs, in the scaly form of systemic demodicosis managed to achieve 100% of the result, but in pustular and mixed form, the effectiveness of the scheme was only 83.3 and 91.9% respectively. In general, the therapeutic efficacy in the group corresponded to 91.9%.

Therefore, in uncomplicated forms of demodicosis, «Simparica®» has the maximum effect, but in more severe forms it is necessary to include drugs of pathogenetic therapies in the treatment, including drugs «Catosal» and «Thioprotectin». When using them in 22-26 days from the beginning of treatment, septic phenomena decreased, the separation of crusts began, the skin became pink; by 30-33 days subcutaneous edema, unpleasant odour, wrinkles disappeared, hair appeared in places of alopecia; up to 45-50 days the skin on the affected areas was clean, smooth, there was an active growth of hair.

5. Conclusion

In generalized demodicosis of dogs, regardless of clinical forms, the best results were obtained when using the acaricide «Simparica®» in combination with the drug «Catosal» – 86.1%, and the acaricide «Simparica®» in combination with drugs «Catosal» and «Thioprotectin» – 91.9%.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

Ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been checked by the authors.

Information about the observance of bioethical standards

Experimental studies were carried out in compliance with the requirements of the Law of Ukraine No. 3447 - IV of February 21, 2006 «On the protection of animals from cruelty» and in accordance with the basic principles of the «European Convention for the Protection of Vertebrate Animals used for Experimental and Scientific Purposes» (Strasbourg, 1986), National Congress on Bioethics «General moral principles of experiments on animals» (Kiev, 2001).

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