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Analysis of pathogenetic manifestation of decompensated intestinal dysbacteriosis in cats

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Abstract. Despite the creation of more and more new generations of antibacterial agents, the correction of intestinal dysbiosis in animals currently remains one of the most complex and urgent problems in clinical veterinary medicine. The article presents an analysis of the pathogenetic manifestation (microbial background, hematological analytes) in decompensated intestinal dysbacteriosis in domestic cats in the dynamics of its correction. The aim of the study was to study the comparative effectiveness of various pharmacotherapy regimens for decompensated intestinal dysbacteriosis in cats. The data shows that when correcting decompensated intestinal dysbacteriosis in domestic cats, the most rational treatment regimen is the complex use of Lactobifadol probiotic (contains at least 1.0×10^6 CFU/g of lactic acid bacteria *Lactobacillus acidophilus* LG1-DEP-VGIKI and 8.0×10^7 CFU/g of bifidobacteria *Bifidobacterium adolescentis* B-1-DEP-VGNKI), Vetelact prebiotic (contains lactulose — not less than 50 %), Azoksivet immunomodulator (contains 1.5 mg of azoximer bromide in 1 ml), as well as infusion therapy (intravenous drip injection of 10 ml/kg of 0.9 % sodium chloride solution; 10 ml/kg of 5 % glucose solution; 5 ml/kg of rheosorbelacl and 2.5 ml/kg of refortan). This was confirmed by the results of pathogenetic picture (analysis of the microbial background and individual hematological analytes), in the dynamics of pharmacotherapy, namely before the start of correction, as well as on days 7 and 14. The improvement of diagnostic approaches and methods for correcting the most severe degree of intestinal dysbacteriosis (the stage of decompensation) creates prerequisites for the future study of dysbiotic disorders of the intestinal tract in other animal species, considering the severity of its manifestation.

Keywords: dysbiosis, small pets, therapy, decompensation, probiotics, prebiotics, immunostimulants

Conflicts of Interest. The drugs were purchased in veterinary pharmacies by the owners of the animals, after they were prescribed by veterinarians in veterinary clinics.

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Data Availability: The data presented in this study are available on request from the corresponding author.

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Introduction

Clinical practice shows that unfavorable environmental factors, malnutrition, violations of veterinary and sanitary standards of maintenance, non-compliance with preventive vaccination cards for infectious diseases and empirical antibiotic therapy leads to immunoreactivity decrease, and, as a result, various immunodeficiency states may occur [1–4]. Moreover, reduction of indigenous microbiota in organism biotopes results in activating growth and development of opportunistic microflora, and pathogenic strains may appear [2, 5–9]. Change in ecological balance of microbiocenosis can change the rules of microecological systems formatting. It leads to the possible development of non-standard microorganism combinations in biotopes, which will contribute to emergence of new complex poor quality microbiocenoses [7, 10–13]. Features of intestinal dysbacteriosis in animals, blurred clinical picture, heterogeneity of symptoms, a wide range of etiological factors create significant difficulties in diagnosis, and the development of this syndrome is often overlooked by veterinary specialists [3, 6, 14]. Therefore, correction of intestinal dysbiosis in animals, including cats, remains one of the most complex and urgent problems of practical veterinary activity.

In recent decades, a steady increase in pathologies accompanied by disorders of gastrointestinal tract of various etiology has been recorded in small domestic animals [9, 15]. However, despite the creation of new antibacterial drugs, probiotics, phytobiotics and prebiotics, the incidence of dysbacteriosis in various pathological processes is constantly growing due to miscalculations in timely diagnosis [2, 16, 17]. Hence, optimization and improvement of diagnostic approaches, as well as the proposal of new effective schemes for correcting intestinal dysbacteriosis of the most severe decompensated degree in cats are an important area of scientific research in veterinary gastroenterology.

The aim of the research was to study the comparative effectiveness of various pharmacotherapy regimens for decompensated intestinal dysbacteriosis in cats.

Materials and methods

The studies were carried out on the basis of the Department of Veterinary Medicine, Peoples' Friendship University of Russia, in 2018–2022. The clinical part of the research

was performed at private veterinary medicine clinics: *Avettura*, *Epiona* and *In the World with Animals*.

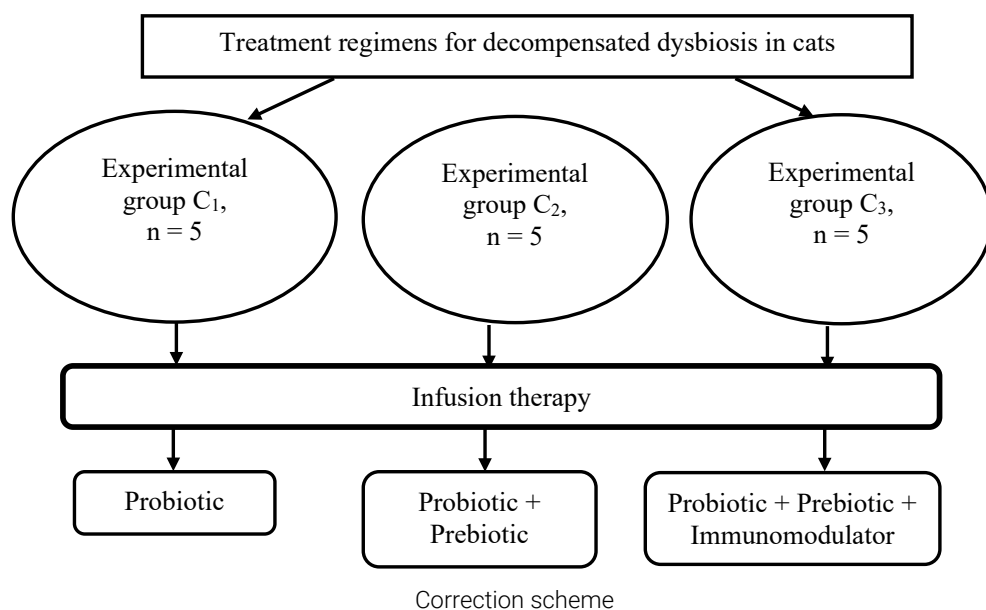
The diagnosis of suspected intestinal dysbacteriosis was made in a complex manner based on the data of anamnesis, clinical examination and microbiological studies. The severity of intestinal dysbacteriosis (compensated, subcompensated, decompensated) was assessed based on clinical and laboratory studies. The controls were clinically healthy mixed-sex individuals ($n = 6$) aged 2...6 years, which were examined with the written consent of their owners before routine vaccination.

Microbiological studies were carried out by conventional methods. Blood samples in EDTA were analyzed on a Mythic 18 automated hematological analyzer with veterinary software (C2 DIAGNOSTICS S.A., France). The functional indicator of hematopoiesis and cellular elements was calculated — the erythrocyte load coefficient (ELC), which was determined by the formula:

$$\text{ELC} = \text{ESR} \times 10 \div \text{Hb},$$

where ESR is erythrocyte sedimentation rate; 10 is a radical element that exhibits the analyzed function; Hb is hemoglobin.

Cats with decompensated intestinal dysbacteriosis admitted to veterinary clinics by 'envelope method' were randomly divided into three experimental groups: C_1 ($n = 5$); C_2 ($n = 5$) and C_3 ($n = 5$). The study design is shown in the figure.



Animals of all experimental groups underwent pathogenetic therapy according to indications and were prescribed Lactobifadol probiotic (contains at least 1.0×10^6 CFU/g of lactic acid bacteria *Lactobacillus acidophilus* LG1-DEP-VGIKI and 8.0×10^7 CFU/g of bifidobacteria *Bifidobacterium adolescentis* B-1-DEP-VGNKI) at a dose of 0.2...0.4g/kg of animal weight once a day for 14 days. Animals of the second experimental group received

Lactobifadol probiotic and Vetelact prebiotic (contains lactulose — not less than 50 %) at the rate of 0.1 ml/kg of animal weight daily for 14 days. Cats of the third experimental group were prescribed Lactobifadol probiotic, Vetelact prebiotic and Azoksivet immunomodulator (contains 1.5 mg of azoximer bromide in 1 ml), which was administered subcutaneously or intravenously once per day for 7 days, at a dose of 0.3 mg/kg live weight. In animals from C₁—C₃ experimental groups, according to indications, infusion therapy consisted of intravenous drip injection — 10 ml/kg of 0.9 % sodium chloride solution; 10 ml/kg of 5 % glucose solution; 5 ml/kg of rheosorbelaact and 2.5 ml/kg of refortan.

Statistical analysis and interpretation of the obtained data were carried out using the computer program STATISTICA 7.0 (StatSoft, USA). At the same time, arithmetic mean (Mean) and standard error (SE) were determined, and standard deviation (SD) was also calculated. After statistical analysis, reliability of the difference between the indices of the experimental groups was determined before and after pharmacological correction, which was calculated using the Mann—Whitney method.

Results and discussion

The approach to correcting intestinal dysbiosis should be comprehensive, considering the causes of its occurrence, restoring the resulting gap in the microbial biotope, creating favorable conditions for reproduction and colonization of indigenous microflora, and also stimulating the immunological response of sick animal. Thus, when correcting the intestinal microbiota in cats, we studied the effectiveness of probiotic, the combined effect of probiotic and prebiotic, as well as the complex action of probiotic, prebiotic, and immunomodulator. The effectiveness of therapy for decompensated intestinal dysbacteriosis in cats was determined by changes in the clinical picture during correction, the results of which are shown in Table 1.

Table 1

Effectiveness of therapy for decompensated intestinal dysbacteriosis in cats

Clinical manifestation	1st experimental group	2nd experimental group	3rd experimental group
Normalization of appetite, days	8.80 ± 0.37	8.20 ± 0.37	7.40 ± 0.24*
Normalization of odor from the oral cavity, days	7.40 ± 0.24	6.60 ± 0.24	5.80 ± 0.20**
Stool normalization, days	7.00 ± 0.31	6.20 ± 0.20	5.20 ± 0.20**
General clinical improvement, days	10.00 ± 0.31	9.20 ± 0.20	7.80 ± 0.20***

Note. *p < 0.05; **p < 0.01; ***p < 0.001.

All three therapeutic regimens that were used in cats with decompensated intestinal dysbacteriosis showed their effectiveness, which clearly confirms the overall clinical improvement in animals of C₁—C₃ experimental groups by 10.00 ± 0.31, 9.20 ± 0.20 and 7.80 ± 0.20 days, respectively. It should be noted that the most effective scheme for correcting the most severe third degree of intestinal dysbacteriosis in cats is the scheme that was prescribed to animals of group C₁. Therefore, in the animals of the third experimental

group, normalization of appetite, odor from the oral cavity, texture of feces and general clinical improvement occurred 1.18 times ($p < 0.05$); 1.27 times ($p < 0.01$); 1.34 times ($p < 0.01$) and 1.28 times ($p < 0.001$), respectively, faster when compared with group C_1 .

The animal organism and its microflora, including intestinal microbiota, are a balanced ecological system. Hence, any qualitative or quantitative changes in microbial biocenosis will undoubtedly have a significant impact on the entire system of homeostasis as a whole. In this regard, to reveal the causes of disorders of intestinal tract, the results of bacteriological research are of decisive importance [3, 4]. For the most objective control of the effectiveness of the correction of intestinal dysbiosis in cats, we conducted microbiological studies of animal feces samples before therapy, as well as on the 7th and 14th days in the dynamics of their treatment.

The results of microbiological studies during the treatment of cats with decompensated intestinal dysbacteriosis of C_1 — C_3 experimental groups are shown in Tables 2–4.

Table 2

Comparison results of intestinal microbiota from cats of group C_1 with decompensated dysbacteriosis, Ig

Genus of microorganism	Before correction	During correction	
		7 days	14 days
<i>Lactobacillus sp. p.</i>	4.47 ± 0.49	7.37 ± 0.25***	9.11 ± 0.20***
<i>Bifidobacterium sp. p.</i>	4.05 ± 0.54	6.96 ± 0.50**	9.26 ± 0.24***
<i>Staphylococcus sp. p.</i>	7.71 ± 0.53	5.66 ± 0.38*	3.57 ± 0.25***
<i>Streptococcus sp. p.</i>	7.31 ± 0.74	5.15 ± 0.63	3.60 ± 0.49**
<i>Escherichia sp. p.</i>	8.39 ± 0.50	7.83 ± 0.32	7.54 ± 0.27
<i>Pseudomonas sp. p.</i>	4.30 ± 1.05	1.72 ± 0.55	0.89 ± 0.42*
<i>Klebsiella sp. p.</i>	7.63 ± 0.81	4.44 ± 0.55*	2.29 ± 0.39***
<i>Citrobacter sp. p.</i>	6.93 ± 0.60	4.51 ± 0.37**	3.15 ± 0.17***
<i>Enterobacter sp. p.</i>	7.21 ± 0.59	4.69 ± 0.45**	3.27 ± 0.39***
<i>Bacillus sp. p.</i>	6.35 ± 0.46	4.65 ± 0.31*	2.68 ± 0.32***
<i>Proteus sp. p.</i>	4.96 ± 0.97	2.50 ± 0.64	1.09 ± 0.48**
<i>Candida sp. p.</i>	6.28 ± 0.26	2.99 ± 0.30***	1.20 ± 0.36***

Note. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 3

Comparison results of intestinal microbiota from cats of group C_2 with decompensated dysbacteriosis, Ig

Genus of microorganism	Before correction	During correction	
		7 days	14 days
<i>Lactobacillus sp. p.</i>	2.81 ± 1.15	7.75 ± 0.44**	9.19 ± 0.25***
<i>Bifidobacterium sp. p.</i>	1.70 ± 0.73	7.93 ± 0.37***	9.85 ± 0.32***
<i>Staphylococcus sp. p.</i>	5.85 ± 1.54	3.97 ± 1.06	2.36 ± 0.84
<i>Streptococcus sp. p.</i>	6.03 ± 1.54	4.18 ± 1.06	2.41 ± 0.63

End of table 3

Genus of microorganism	Before correction	During correction	
		7 days	14 days
<i>Escherichia sp. p.</i>	8.03 ± 0.43	7.71 ± 0.31	7.55 ± 0.21
<i>Pseudomonas sp. p.</i>	2.65 ± 1.65	0	0
<i>Klebsiella sp. p.</i>	4.97 ± 2.03	2.24 ± 0.95	0*
<i>Citrobacter sp. p.</i>	5.79 ± 1.54	3.23 ± 0.98	2.02 ± 0.63
<i>Enterobacter sp. p.</i>	4.00 ± 1.66	2.75 ± 1.16	3.12 ± 0.45
<i>Bacillus sp. p.</i>	4.20 ± 1.75	2.56 ± 1.06	2.39 ± 0.99
<i>Proteus sp. p.</i>	3.74 ± 1.55	1.19 ± 0.52	0*
<i>Candida sp. p.</i>	3.90 ± 1.67	1.94 ± 0.81	0.92 ± 0.41

Note. *p < 0.05; ** p < 0.01; *** p < 0.001.

Table 4

**Comparison results of intestinal microbiota from cats of group C₃
with decompensated dysbacteriosis, Ig**

Genus of microorganism	Before correction	During correction	
		7 days	14 days
<i>Lactobacillus sp. p.</i>	1.84 ± 1.17	8.19 ± 0.46**	8.67 ± 0.35***
<i>Bifidobacterium sp. p.</i>	0.47 ± 0.47	9.15 ± 0.39***	9.91 ± 0.39***
<i>Staphylococcus sp. p.</i>	1.36 ± 1.36	2.03 ± 0.89	1.90 ± 0.80
<i>Streptococcus sp. p.</i>	7.68 ± 0.52	4.17 ± 0.23***	3.27 ± 0.33***
<i>Escherichia sp. p.</i>	8.19 ± 0.50	6.95 ± 0.49	6.84 ± 0.23*
<i>Pseudomonas sp. p.</i>	6.58 ± 0.30	0***	0***
<i>Klebsiella sp. p.</i>	6.22 ± 0.55	2.20 ± 0.40***	0***
<i>Citrobacter sp. p.</i>	3.26 ± 2.00	1.53 ± 0.71	1.42 ± 0.65
<i>Enterobacter sp. p.</i>	2.98 ± 1.85	1.79 ± 0.89	1.57 ± 0.76
<i>Bacillus sp. p.</i>	1.73 ± 1.73	1.53 ± 0.68	1.48 ± 0.60
<i>Proteus sp. p.</i>	0	0	0
<i>Candida sp. p.</i>	3.57 ± 2.19	0	0

Note. *p < 0.05; ** p < 0.01; *** p < 0.001.

The comparison results (Tables 1–4) indicate that during the treatment of domestic cats with the third degree of decompensation of intestinal dysbacteriosis of C₁—C₃ experimental groups, in fecal samples taken for bacteriological studies, a significant increase in the number of representatives of *Lactobacillus sp. p.* by 1.64 (p < 0.001), 2.75 (p < 0.01) and 4.45 times (p < 0.01), respectively, was noted already on the seventh day of corrective treatment period, compared with output indicators. On the 14th day of therapy in animals of C₁, C₂ and C₃ experimental groups, a highly significant (p < 0.001) increase in the number of lactobacilli by 2.03, 3.27 and 4.71 times, respectively, was observed in fecal samples, when compared with the original data. A similar positive trend was observed when analyzing the amount of bifidobacteria in fecal samples of cats with decompensated intestinal dysbacteriosis during their therapy. Thus, on the 14th day of pharmacotherapy, a highly significant

($p < 0.001$) increase in *Bifidobacterium* sp. p. was observed in fecal samples in cats of C_1 , C_2 and C_3 experimental groups (by 2.28 times — from 4.05 ± 0.54 to 9.26 ± 0.24 lg; by 5.79 times — from 1.70 ± 0.73 to 9.85 ± 0.32 lg and by 21.08 times — from 0.47 ± 0.47 to 9.91 ± 0.39 lg, respectively). In addition, already on the 7th day of therapy in animals of group C_3 , a significant decrease in the number of streptococci by 1.84 times ($p < 0.001$), *Klebsiella* by 2.82 times ($p < 0.001$), a complete absence of *Pseudomonas* and *Candida* was observed. Positive dynamics was observed in animals of this group on the 14th day of therapy, which was accompanied by the absence of *Klebsiella* isolation.

When making a diagnosis, in addition to a detailed analysis of intestinal microbiocenosis, it is also necessary to consider pathogenetic features of dysbiosis, which will make it possible to most accurately diagnose, determine the severity of pathology, predict its further course, and also select the optimal tactics for therapeutic correction [16]. The dynamics of changes in hematological analytes of cats with decompensated intestinal dysbacteriosis, in the course of their therapy, is shown in Tables 5–7.

Table 5

Dynamics of hematological analytes of cats of group C_1 with decompensated dysbacteriosis during therapy

Indicators	Before correction	During correction	
		7 days	14 days
Hemoglobin, g/l	101.80 ± 5.04	115.20 ± 3.89	$128.80 \pm 1.90^{**}$
ESR, mm/h	26.40 ± 2.52	$13.60 \pm 1.02^{**}$	$6.00 \pm 0.44^{***}$
ELC, cond. units	2.61 ± 0.27	$1.17 \pm 0.07^{**}$	$0.46 \pm 0.02^{***}$
Leukocytes, g/l	16.42 ± 1.02	$10.94 \pm 0.57^{**}$	$9.16 \pm 0.30^{***}$

Note. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 6

Dynamics of hematological analytes of cats of group C_2 with decompensated dysbacteriosis during therapy

Indicators	Before correction	During correction	
		7 days	14 days
Hemoglobin, g/l	100.40 ± 3.95	$123.00 \pm 4.32^{**}$	$136.40 \pm 2.94^{***}$
ESR, mm/h	22.60 ± 4.00	$10.20 \pm 0.86^*$	$4.80 \pm 0.66^{**}$
ELC, cond. units	2.27 ± 0.40	$0.82 \pm 0.06^{**}$	$0.34 \pm 0.04^{**}$
Leukocytes, g/l	20.30 ± 1.23	$11.38 \pm 0.50^{***}$	$8.48 \pm 0.29^{***}$

Note. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 7

Dynamics of hematological analytes of cats of group C_3 with decompensated dysbacteriosis during therapy

Indicators	Before correction	During correction	
		7 days	14 days
Hemoglobin, g/l	102.20 ± 4.59	$137.20 \pm 2.63^{***}$	$145.20 \pm 2.35^{***}$
ESR, mm/h	23.80 ± 2.59	$6.00 \pm 0.70^{***}$	$3.80 \pm 0.37^{***}$
ELC, cond. units	2.34 ± 0.27	$0.43 \pm 0.04^{***}$	$0.25 \pm 0.02^{***}$
Leukocytes, g/l	17.64 ± 0.53	$9.82 \pm 0.44^{***}$	$8.40 \pm 0.29^{***}$

Note. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

It was found that the most positive changes in hematological parameters were recorded in cats of C₃ experimental group. Thus, in domestic cats of the third experimental group, a highly significant increase in the amount of hemoglobin by 1.34 times ($p < 0.001$) was recorded already on the seventh day of correction, against the background of a significant decrease in the ESR indicator by 3.96 times ($p < 0.001$), the ELC indicator by 5.44 times ($p < 0.001$) and the level of leukocytes by 1.79 times ($p < 0.001$), when compared with hematological parameters before the therapy. Further observation of experimental animals confirms the effectiveness of the correction of group C₃ animals. Thus, on the 14th day of complex pharmacocorrection of domestic cats with probiotic, prebiotic and immunomodulator, it led to a further increase in hemoglobin levels by 1.42 times ($p < 0.001$), a decrease in ESR by 6.26 times ($p < 0.001$), from 23.80 ± 2.59 to 3.80 ± 0.37 mm/h; indicator of ELC by 9.36 times ($p < 0.001$), from 2.34 ± 0.27 to 0.25 ± 0.02 cond. units and the level of leukocytes by 2.10 times ($p < 0.001$), from 17.64 ± 0.53 to 8.40 ± 0.29 g/l, compared with the indices of experimental cats before treatment.

The results of the research revealed the mechanisms of formation of intestinal microbiocenosis in the most severe decompensated degree in domestic cats, diagnostic approaches were improved through a detailed clinical analysis and correction of dysbiosis. It was established that determining the severity of the course of intestinal dysbiosis in cats during diagnosing has a certain prognostic value, which ultimately can affect the most optimal choice of therapeutic correction. The introduction of Lactobifadol probiotic, Vetelact prebiotic and Azoksivet immunomodulator into the therapeutic schemes for correction of decompensated intestinal dysbacteriosis in cats turned out to be pathogenetically justified.

Conclusion

Clinical and diagnostic approaches have been scientifically substantiated, as well as methods for correcting decompensated intestinal dysbacteriosis in cats have been improved. Thus, using Lactobifadol (0.2...0.4 g/kg) in combination with Vetelact (0.1 ml/kg), Azoksivet (3 mg/kg) and infusion therapy (intravenous drip injection of 10 ml/kg of 0.9 % sodium chloride solution; 10 ml/kg of 5 % glucose solution; 5 ml/kg of rheosorbelaact and 2.5 ml/kg of refortan) in cats with decompensated intestinal dysbacteriosis for 7 days was the most effective. This was evidenced by the registration of a general clinical improvement 1.28 times faster, as well as the normalization of appetite, halitosis, texture of feces in cats of the third experimental group by 1.40; 1.60 and 1.80 days earlier compared to sick cats of the first experimental group.

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Анализ патогенетической манифестации декомпенсированного дисбактериоза кишечника у кошек

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Аннотация. Несмотря на создание новых поколений антибактериальных средств, коррекция дисбиоза кишечника у животных остается одной из самых сложных и актуальных проблем в клинической ветеринарной медицине. Приведен анализ патогенетической манифестации (микробный фон, гематологические анализы) при декомпенсированном дисбактериозе кишечника у домашних кошек в динамике его коррекции. Цель исследования — изучить сравнительную эффективность различных схем фармакотерапии декомпенсированного дисбактериоза кишечника у кошек. Показано, что при коррекции декомпенсированного дисбактериоза кишечника у домашних кошек наиболее рациональной схемой терапии является комплексное применение пробиотика «Лактобифадол» (действующие вещества: лактобактерии *Lactobacillus acidophilus* и бифидобактерии *Bifidobacterium adolescentis*), пребиотика «Ветелакт» (содержит лактулозу — не менее 50 %), иммуномодулятора «Азоксивет» (Азоксимер бромид), а также инфузионной терапии (натрия хлорида 0,9 % раствор, в/в, капельно, в дозе 10 мл/кг; 5 % раствор глюкозы, в/в, капельно, в дозе 10 мл/кг; раствор реосорбелакта, в/в, капельно, в дозе 5 мл/кг; раствор рефортана, в/в, капельно, в дозе 2,5 мл/кг живой массы тела). Это подтверждено результатами патогенетической картины (анализ микробного фона и отдельных гематологических анализов) в динамике фармакотерапии: до начала коррекции, на 7-е и 14-е сутки. Совершенствование диагностических подходов и методов коррекции наиболее тяжелой степени дисбактериоза кишечника (стадия декомпенсации) создают предпосылки для будущего изучения дисбиотических нарушений кишечного тракта у других видов животных с учетом стадийности тяжести его проявления.

Ключевые слова: дисбиоз, мелкие домашние животные, терапия, декомпенсация, пробиотики, пребиотики, иммуностимуляторы

Заявление о конфликте интересов. Авторы заявляют об отсутствии конфликта интересов. Препараты приобретались в ветеринарных аптеках владельцами животных, после их назначения ветеринарными врачами в ветеринарных клиниках.

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