Features of the course of compensated, subcompensated and decompensated intestinal dysbiosis in cats

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Abstract. The study of intestinal dysbiosis in animals remains one of the most complex and urgent problems in veterinary medicine to this day. Recently, a steady increase in pathologies has been recorded, accompanied by the development of disorders of the gastrointestinal tract of various etiologies in animals. Despite the constant improvement of methods for correcting the intestinal microbiota, the occurrence of dysbacteriosis in various pathological processes not only does not decrease, but, on the contrary, increases. This study revealed definite pathogenetic features of intestinal dysbiosis in cats of varying severity. It has been established that substantial changes occur in the blood of cats with dysbiosis, and with the decompensated third degree of severity, profound hematological shifts occur. The differences found may have significant clinical and laboratory importance since they complement the available data on intestinal dysbiosis in cats, which, in our opinion, will improve diagnostic and prognostic approaches, as well as therapeutic and preventive measures. Keywords: dysbiosis, cats, pathogenesis, compensated, subcompensated, decompensated.

1 Introduction

Under the influence of a number of environmental factors, unsatisfactory nutrition, violations of elementary veterinary and sanitary rules of keeping, failure to take measures to prevent infectious diseases, and irrational antibiotic therapy, the immunocompetent system can suffer, and as a result, various immunodeficiency states arise [1-4]. As a result, not only conditionally pathogenic microflora, but even saprophytic microorganisms are activated [1, 3, 5]. This situation creates ample opportunities for the formation of various combinations of microorganisms in the biotopes of the body, leading to the emergence of complex and often poor-quality microbiocenoses [6-9].
The problem of dysbiosis has become especially relevant in small domestic animals due to the urbanization of the population, the growth of the economic and social development of society, while this syndrome is the most common manifestation of intestinal microbiome disorders in animals, and its development is always accompanied by the subsequent development of metabolic and immunological disorders [7, 10-14]. At the same time, this pathology remains a daily practice of veterinary institutions and is characterized by various manifestations, as well as great interest from the scientific community [8, 15-18]. The peculiarity of the manifestation of dysbiosis presents a significant difficulty since this pathology, without a clear clinical manifestation, is often recognized by the doctor as insignificant, while the already developing pathological process is overlooked [19-23].

Intestinal dysbiosis in cats is quite common, however, at present, there are no scientifically based data on the pathogenetic features of the course of this syndrome, which is why there are no diagnostic and therapeutic protocols for various degrees of severity of its course [12, 24-29]. Therefore, the spread of this syndrome and the pathogenetic diversity of the course of intestinal dysbiosis in cats determine the need for a radical improvement in diagnostic approaches. Previously, we conducted and published a detailed analysis of the characteristics of the fecal microbiota in cats with compensated, subcompensated, and decompensated intestinal dysbiosis [6, 10, 17, 30-35].

Clinicians often do not consider the etiological role in the occurrence of gastrointestinal disorders in animals during the initial examination, which leads to errors in the diagnosis and incorrect methods of subsequent drug treatment [4, 17, 36-38]. Currently, the available literature lacks information on diagnostic approaches for intestinal dysbiosis in cats of varying severity. Therefore, the development of diagnostic criteria and approaches for various scenarios of the development of the pathological process, in our opinion, is an important area of scientific research in veterinary medicine, which will undoubtedly lead to the improvement of methods of correcting intestinal dysbiosis in cats.

This study aimed to compare individual hematological analytes in cats with intestinal dysbiosis of varying severity.

2 Materials and methods

The studies were conducted during the period 2019-2021, based on private veterinary clinics: "Avettura," "Epiona" (Moscow city), and "In the world with animals" (Serpukhov city). Cats’ examination and biomaterial sampling for the research was carried out following the International Bioethical Standards, the provisions of the IV European Convention "On the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (ETS 123, 1986), and the Russian Federation legislative documents for conducting experiments on animals. Study cats were chosen as they entered the veterinary clinics for the first time. The diagnosis was established comprehensively, considering the anamnesis data, clinical examination, and microbiological studies. The experiment involved 46 adult animals, ranging from 2 to 6 years old, of mixed genders with intestinal dysbiosis syndrome. All cats were kept in apartments in urban conditions. Depending on the degree of severity of intestinal dysbiosis, animals were divided into the following groups: group 1 - cats with the first degree of intestinal dysbiosis (n = 15); group 2 - cats with the second degree of intestinal dysbiosis (n = 16); group 3 - cats with the third degree of intestinal dysbiosis (n = 15). Clinically healthy individuals served as control (n = 6) aged 2-6 years old, also of mixed genders, which were examined with the consent of their owners before routine vaccination. The cats were fed three times a day "Purina Pro Plan," a commercial dry balanced adult animal feed.
Based on the clinical and laboratory studies, the severity of intestinal dysbiosis was assessed (1st degree - compensated; 2nd degree - sub-compensated; 3rd degree - decompensated).

At the first degree (compensated) of intestinal dysbiosis in cats: the level of consciousness was within the normal range; in most cases, it was accompanied by constipation, often - the appearance of halitosis, in rare cases - a decrease in appetite and dryness of the skin, no signs of dehydration, body temperature is within normal limits.

Intestinal dysbiosis of the second degree (sub-compensated) in cats: level of consciousness was slight depression; there was halitosis, dryness of the skin and mucous membranes were often manifested, as well as hyporexia, accompanied by constipation and diarrhea, in rare cases, alternating constipation and diarrhea. There was dehydration within 5%, with a possible slight increase in body temperature.

Intestinal dysbiosis of the third (decompensated) degree in cats: the level of consciousness was depressed; necessarily the presence of anorexia, halitosis, dryness of the skin and mucous membranes, and pruritus were also possible. In most cases, it was accompanied by alternating constipation and diarrhea; in some cases, diarrhea. Dehydration was within 10%, with a possibility of an increase in body temperature or hypothermia.

Blood samples in EDTA were analyzed using an automated hematology analyzer (Mythic 18) with veterinary software (C2 DIAGNOSTICS S.A., France) to measure the following parameters: hemoglobin level (Hb), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), lymphocyte count (LYM). In addition, the functional indicator of hematopoiesis and cellular elements - erythrocyte load ratio (ELR) was determined. The erythrocyte load ratio (ELR) is a relative index that allows judging the erythropoiesis intensity, the level of hemoglobin, and, indirectly, the oxygen supply of the body, as well as the elimination of carbon dioxide and the severity of the inflammatory process. The ELR was determined by the following formula:

$$ELR = \frac{ESR \times 10}{Hb},$$

The obtained results were statistically analyzed using the statistical program STATISTICA 7.0 (StatSoft, USA) and presented in tables and figures. The arithmetic mean, mean square error (SE), and standard deviation (SD) were calculated. The reliability of the difference in indicators between the control and experimental groups indicators was calculated using the Mann-Whitney test (* - p <0.05; ** - p <0.01; *** - p <0.001).

3 Results and discussion

The study involved 46 adult animals, aged 2-6 years, of mixed genders, with intestinal dysbiosis syndrome.

In 15 out of 46 sick cats (32.6%), the clinical picture of the disease was characterized by clear consciousness, normothermia, normal appetite, the animals actively and voluntarily changed their pose and moved freely in space, vomiting, and signs of dehydration were not registered. At the same time, eleven individuals (73.3%) had halitosis, three (20.0%) had a decrease in appetite, and two (13.3%) had dry skin and mucous membranes. When analyzing the nature of the stool in cats with the first degree of dysbiosis, it was found that thirteen animals (86.7%) had constipation, and in two was noted the presence of formed feces with uneven coloring. In this case, we diagnosed a compensated course of intestinal dysbiosis (group 1).

In 16 out of 46 sick cats (34.8%), subcompensated intestinal dysbiosis was recorded, the clinical manifestations of which were halitosis (93.7%), anorexia, dry skin, and mucous membranes (50.0% each). When analyzing the nature of the stool, it was found that eight animals (62.5%) had constipation, five (31.3%) had liquid feces, and three animals (6.3%) had diarrhea. In some cases, diarrhea was accompanied by alternating constipation and diarrhea. Dehydration was within 5%, with a possible slight increase in body temperature or hypothermia.

ELR = \frac{ESR \times 10}{Hb}$,
had alternating constipation and diarrhea. In cats with loose stools, the frequency of defecation was 3–4 times per day. Signs of dehydration for this stage of dysbiosis are insignificant. In most cases, clinical methods in cats with dysbiosis of the second degree of severity revealed a slight weakness, also noted hyporexia at normal body temperature. According to the indicated clinical picture of the disease, we stated the presence of a subcompensated course of intestinal dysbiosis in cats (group 2).

When comparing the clinical signs of dysbiosis in 15 of 46 sick cats (32.6%), the clinical picture was manifested by dry skin and mucous membranes, hyporexia, and halitosis. In addition, five cats (33.3%) had pruritus, four (26.7%) had diarrhea, and eleven (73.3%) had diarrhea alternating with constipation. It has been established that constipation was not recorded in cats with decompensated dysbiosis. It should be emphasized that pruritus at the 1st and 2nd degrees of severity of dysbiosis did not occur. It should be noted that in the group of cats with decompensated dysbiosis, the pathology of the gastrointestinal tract manifested itself in the form of severe depression; liquid or unformed feces were noted, while the frequency of defecation was 5–10 times a day. An increase in the signs of dehydration and intoxication was also noted, characterized by the forced lying position of animals, hyporexia, or anorexia. These signs allowed us to determine the decompensated course of intestinal dysbiosis in cats (group 3).

Etiological verification depending on the degree of intestinal dysbiosis manifestation in cats is shown in Figure 1.

**Fig. 1.** Etiological verification of dysbiosis in cats (n = 46), depending on its severity.
The relationship between the focus of inflammation and the whole organism is obviously traced by the hematological blood parameters. Therefore, studying the hematological analytes during intestinal dysbiosis is one of the most informative methods for assessing the severity of its clinical course. To complete the picture of intestinal dysbiosis’s clinical and laboratory characteristics in cats of varying severity, we have revealed certain pathogenetic features of this syndrome course. The levels of particular hematological parameters (Hb, ESR, ELR, IRI) in the blood of cats with intestinal dysbiosis are shown in Figure 2.

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<th>2 group</th>
<th>3 group</th>
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<tr>
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<td>130</td>
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<tr>
<td><strong>ESR, mm/h</strong></td>
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<tr>
<td><strong>IRI, con. units</strong></td>
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<td>1,0</td>
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Note: Mean – the arithmetic mean; SE - standard error; SD - standard deviation; *** - the reliability of the difference between the experimental and control groups (Mann-Whitney test).

**Fig. 2.** The level of individual hematological parameters (Hb, ESR, ELR, IRI) in the blood of cats with intestinal dysbiosis of varying severity. The presented data in (Fig. 2. A) indicate that anemia occurs with intestinal dysbiosis, which is aggravated depending on the degree of severity, and with decompensated dysbiosis (3rd degree of severity), it illustrates its maximum values. In animals with the 1st degree of intestinal dysbiosis, the hemoglobin level in the blood significantly decreased (p <0.001) by 1.12 times, from 145.83 ± 3.78 to 129.46 ± 1.92 g/L; significantly decreased (p <0.001) by 1.31 times, from 145.83 ± 3.78 to 111.06 ± 2.25 g/L in animals with the 2nd degree of dysbiosis; and highly significant decreased (p <0.001) by 1.43 times, from 145.83 ± 3.78 to 101.46 ± 2.44 g/L in animals with decompensated intestinal dysbiosis, when compared with healthy clinical cats.
Moreover, the erythrocyte sedimentation rate was measured in healthy cats and animals with dysbiosis of varying severity. The results are shown in (Fig. 2. B). Figure data show that, with intestinal dysbiosis, a highly significant increase in ESR is observed. Consequently, in cats with the first, second, and third degrees of compensation of intestinal dysbiosis, we recorded a highly significant increase in ESR (p <0.001) by 2.03 times, from 3.50 ± 0.42 to 7.13 ± 0.52 mm/h; by 4.46 times, from 3.50 ± 0.42 to 15.62 ± 0.88 mm/h and by 6.93 times, from 3.50 ± 0.42 to 24.26 ± 1.71 mm/h, respectively when compared with animals of the control group.

As a functional analysis of the hemogram of cats with intestinal dysbiosis, we calculated the ELR indicator (Fig. 2. C). The data presented in the figure indicate that a significant increase in ELR was observed in cats with intestinal dysbiosis. This indicator increased with high significance (p <0.001) in cats with intestinal dysbiosis: with 1st degree, increased by 2.29 times, from 0.24 ± 0.03 to 0.55 ± 0.04 conventional units; with 2nd degree, by 5.91 times, from 0.24 ± 0.03 to 1.42 ± 0.09 conv. units; and in cats with the 3rd degree of dysbiosis, by 10.0 times, from 0.24 ± 0.03 to 2.41 ± 0.17 conv. units, when compared with the indicators of control animals.

Clinical examination of 46 cats with intestinal dysbiosis syndrome revealed that the compensated degree of dysbiosis was accompanied by halitosis, constipation, anorexia, and dryness of the external integument. With a subcompensated degree, halitosis, dry skin and mucous membranes, and reduced appetite, accompanied by constipation or diarrhea, in rare cases, alternating constipation and diarrhea are observed. Decompensated degree of intestinal dysbiosis is accompanied by decreased appetite, halitosis, dry skin and mucous membranes, pruritus, alternating constipation and diarrhea, and in some cases, only diarrhea. These data were obtained for the first time and complement our previously published microbiological characterization of the qualitative and quantitative composition of the intestinal microbiome in compensated, subcompensated, and decompensated intestinal dysbiosis in cats.

Blood hemoglobin is involved in oxygen and carbon dioxide transport and maintains pH balance, which is an essential indicator of a general blood test [39, 40]. The data obtained indicate that with intestinal dysbiosis, anemia occurs, which is aggravated depending on the severity, and with the third degree of severity, it shows its maximum values. The erythrocyte sedimentation rate (ESR) is an indicator that determines the speed and intensity of erythrocyte agglutination during specific pathological processes; therefore, it is one of the mandatory values of the general blood test. In intestinal dysbiosis, a highly significant increase in the ESR index is also observed; thus, in cats with the first, second, and third degrees of compensation of intestinal dysbiosis, a highly significant increase was recorded in the ESR index, when compared with animals of the control group.

4 Conclusion

In conclusion, intestinal dysbiosis is not a diagnosis but a situation that accompanies the occurrence and development of several pathologies in animals. It is always secondary and due to the corresponding cause; therefore, the diagnosis of intestinal microbiota disorders should be based on the complex application research methods. The peculiarity of the manifestation of dysbiosis in cats is substantially difficult since this pathology, having no clinical specificity, is often recognized by the doctor as insignificant, while the already developing pathological process is overlooked. The symptomatic pool, determined during a detailed clinical examination of a sick animal, has an undeniable diagnostic value. Therefore, the clinician, evaluating the results of collecting anamnesis from the owner of the animal as well as physical examination data, should choose the most objective and specific from a variety of clinical signs. Highlighting one "main" symptom can prompt the doctor to make hasty and ill-considered decisions. To avoid this, the clinician should detect as many clinical
symptoms as possible before making pathogenetic combinations. The results of this study revealed significant pathogenetic differences in cats with intestinal dysbiosis of varying severity. It has been established that significant changes occur in the blood of cats with dysbiosis, and with the decompensated third degree of severity, profound hematological shifts arise. The differences we found have essential clinical and laboratory significance; they complement the available data on intestinal dysbiosis in cats, which, in our opinion, will improve diagnostic and prognostic approaches, as well as treatment and prophylactic measures. Improving approaches to diagnosing and predicting intestinal dysbiosis in cats creates the prerequisites for studying dysbiotic disorders of the intestinal tract in other animal species.

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